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\$0.40 Estimated total session cost 0.008 Hrs.

File 155:MEDLINE 1966-1993/NOV (9311W2)

Set	Items	Description
?s her2 or neu or p185 or c(w)erbb		
	93	HER2
	960	NEU
	106	P185
	345578	C
	1168	ERBB
	542	C(W)ERBB
S1	1441	HER2 OR NEU OR P185 OR C(W)ERBB
?s insulin(w)receptor or (igf or insulin(w)like(w)growth(w)factor) (w)receptor		
	105970	INSULIN
	179748	RECEPTOR
	3217	INSULIN(W)RECEPTOR
	4607	IGF
	105970	INSULIN
	125471	LIKE
	331432	GROWTH
	221383	FACTOR
	6780	INSULIN(W)LIKE(W)GROWTH(W)FACTOR
	179748	RECEPTOR
	264	(IGF OR INSULIN(W)LIKE(W)GROWTH(W)FACTOR) (W)RECEPTOR
S2	3422	INSULIN(W)RECEPTOR OR (IGF OR INSULIN(W)LIKE(W)GROWTH(W)FACTOR) (W)RECEPTOR
?s (egf or epidermal(w)growth(w)factor) (w)receptor		
	6467	EGF
	24654	EPIDERMAL
	331432	GROWTH
	221383	FACTOR
	10864	EPIDERMAL(W)GROWTH(W)FACTOR
	179748	RECEPTOR
S3	3037	(EGF OR EPIDERMAL(W)GROWTH(W)FACTOR) (W)RECEPTOR
?s s1 or s2 or s3		
	1441	S1
	3422	S2
	3037	S3
S4	7537	S1 OR S2 OR S3
?s truncat?		
S5	96317	TRUNCAT?
?s s4 and s5		
	7537	S4
	96317	S5
S6	481	S4 AND S5
?s extracellular or external or surface or ligand(w)binding or hydrophilic or (amino or n)(w)terminal		
	58123	EXTRACELLULAR
	58638	EXTERNAL
	100103	SURFACE

23131 LIGAND  
 289365 BINDING  
 4935 LIGAND(W) BINDING  
 7425 HYDROPHILIC  
 232041 AMINO  
 235640 N  
 80875 TERMINAL  
 21403 (AMINO OR N) (W) TERMINAL  
 S7 313465 EXTRACELLULAR OR EXTERNAL OR SURFACE OR LIGAND(W) BINDING  
 OR HYDROPHILIC OR (AMINO OR N) (W) TERMINAL

?s s6 and s7

481 S6  
 313465 S7  
 S8 153 S6 AND S7

?save temp

Temp SearchSave "TD198" stored

t s8/7/93 96 97 99 100 102 106 108 111 112 116 120 122 125 131 137

8/7/93

07072077 89374077

Secretion of the extracellular domain of the human insulin receptor from insect cells by use of a baculovirus vector.

Sissom J; Ellis L

Howard Hughes Medical Institute, Dallas, TX.

Biochem J Jul 1 1989, 261 (1) p119-26, ISSN 0264-6021

Journal Code: 9Y0

Languages: ENGLISH

Document type: JOURNAL ARTICLE

To explore the utility of the baculovirus/insect-cell system for the expression of a soluble secreted human insulin-receptor (hIR) extracellular ligand-binding domain, we have engineered a recombinant virus encoding an hIR deletion mutant which is truncated eight residues from the beginning of the predicted transmembrane domain (i.e. 921 residues). Within 24 h after infection of Sf9 cells with virus, insulin-binding activity begins to accumulate in the culture medium, and reaches a maximum between 48 and 72 h. The intracellular transit and processing of this secreted receptor, designated 'AchIR01', is quite slow. After 24 h in pulse-chase experiments approximately 50% of the metabolically labelled protein is still inside the cell. This protein accumulates as a non-cleaved hIR precursor which is glycosylated, but the carbohydrate is entirely endoglycosidase H (endoH)-sensitive (i.e. high mannose). Approximately one-half of the receptor in the culture medium (i.e. approximately 25% of the total) is in the form of non-cleaved precursor, and about one half of its carbohydrate chains are now endoH-resistant. The remainder of the protein is proteolytically processed hIR (alpha-plus truncated beta-subunits). None of these hIR species exhibit O-linked carbohydrate. Only the processed form of the receptor in the medium binds insulin. This insulin-binding protein is secreted as a dimer (alpha beta)<sub>2</sub>, and binds insulin with an affinity which is comparable with that of both the wild-type hIR as well as the secreted form of the hIR expressed in mammalian cells. Despite the rather inefficient processing and altered glycosylation of the AchIR01 protein in insect cells, this high-affinity insulin-binding protein accumulates in the medium at levels (mg/litre) of about 100 times that achieved in a mammalian-cell system.

8/7/96

06929614 89231614

A chimeric EGF-R-neu proto-oncogene allows EGF to regulate neu tyrosine kinase and cell transformation.

Lehvaslaiho H; Lehtola L; Sistonen L; Alitalo K

Department of Virology and Pathology, University of Helsinki, Finland.

EMBO J Jan 1989, 8 (1) p159-66, ISSN 0261-4189 Journal Code: EMB

Languages: ENGLISH

The neu oncogene, characterized by Weinberg and colleagues, is a transforming gene found in ethylnitrosourea-induced rat neuro/glioblastomas; its human proto-oncogene homologue has been termed *erbB2* or *HER2* because of its close homology with the epidermal growth factor receptor (EGF-R) gene (*c-erbB1*). Expression of the rat neu oncogene is sufficient for transformation of mouse NIH 3T3 fibroblasts in culture and for the development of mammary carcinomas in transgenic mice, but the neu proto-oncogene has not been associated with cell transformation. We constructed a vector for expression of a chimeric cDNA and hybrid protein consisting of the EGF-R extracellular, transmembrane and protein kinase C-substrate domains linked to the intracellular tyrosine kinase and carboxyl terminal domain of the rat neu cDNA. Upon transfection with the construct, NIH 3T3 cells gave rise to EGF-R antigen-positive cell clones with varying amounts of specific EGF binding. Immunofluorescence and immunoprecipitation using neu- and EGF-receptor specific antibodies demonstrated a correctly oriented and positioned chimeric EGF-R-neu protein of the expected apparent mol. wt on the surface of these cells. EGF or TGF alpha induced tyrosine phosphorylation of the chimeric receptor protein, stimulated DNA synthesis of EGF-R-neu expressing cells and led to a transformed cell morphology and growth in soft agar. In contrast, the neu proto-oncogene did not show kinase activity or transforming properties when expressed at similar levels in NIH 3T3 cells. (ABSTRACT TRUNCATED AT 250 WORDS)

8/7/97

06917061 89219061

Inhibition of tyrosine kinase activity of the epidermal growth factor (EGF) receptor by a truncated receptor form that binds to EGF: role for interreceptor interaction in kinase regulation.

Basu A; Raghunath M; Bishayee S; Das M

Department of Biochemistry and Biophysics, Children's Hospital of Philadelphia, Pennsylvania.

Mol Cell Biol Feb 1989, 9 (2) p671-7, ISSN 0270-7306 Journal Code: NGY

Contract/Grant No.: CA-43787; CA-15822; CA-44441

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The tyrosine kinase activity of the epidermal growth factor (EGF) receptor is regulated by a truncated receptor of 100 kilodaltons (kDa) that contains the EGF-binding site but not the kinase domain. The inhibition of kinase is not due to competition for available EGF or for the kinase substrate-binding site. Chemical cross-linking studies suggest that the 100-kDa receptor may form a heterodimer with the intact EGF receptor. Structurally related receptor kinases, such as the platelet-derived growth factor receptor, the insulin receptor, and the Neu receptor, were not inhibited by the 100-kDa receptor. The results indicate that (i) the inhibition was specific for the EGF receptor, (ii) the kinase domain had little or no role in determining target specificity, and (iii) the regulation of kinase may be due to a specific interaction of the 100-kDa receptor with the ligand-binding domain of the EGF receptor kinase.

8/7/99

06899873 89201873

Analysis of mammalian fibroblast transformation by normal and mutated human EGF receptors.

Haley JD; Hsuan JJ; Waterfield MD

Ludwig Institute for Cancer Research, London, UK.

Oncogene Mar 1989, 4 (3) p273-83, ISSN 0950-9232 Journal Code: ONC

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Activation of the EGF receptor (*c-erbB*) tyrosine kinase has been implicated in tumorigenesis, either by overexpression of the normal receptor in the presence of EGF, or through expression of a truncated receptor lacking the EGF binding domain as in the viral oncogene *v-erbB*. Here, normal and truncated human EGF receptors expressed in Rat1

fibroblasts were analysed for receptor tyrosine kinase activity and several transformation parameters in comparison with polyoma middle T and EJ-ras. Expression of a truncated EGF receptor lacking the extracellular ligand binding domain induced transformation of immortalized rodent fibroblasts and appears to activate the intrinsic tyrosine kinase. The transformed phenotype becomes enhanced by further truncation of the C-terminal domain containing the tyrosine autophosphorylation sites P1 and P2. Over expression of EGF receptors with an intact extracellular region in transfected Rat1 cells shows EGF dependent transformation, which is reduced by C-terminal truncation. Transformation is dependent on the cellular receptor concentration and can be selected as a stable phenotype. We conclude that expression of receptors with a truncated EGF-binding domain alone is sufficient to transform mammalian fibroblasts, in contrast to chick fibroblasts transformed by v-erbB where additional deletion of C-terminal receptor sequences appears to be an absolute requirement.

8/7/100

06860036 89162036

Structure and function of human amphiregulin: a member of the epidermal growth factor family.

Shoyab M; Plowman GD; McDonald VL; Bradley JG; Todaro GJ

Oncogen, Seattle, WA 98121.

Science Feb 24 1989, 243 (4894 Pt 1) p1074-6, ISSN 0036-8075

Journal Code: UJ7

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The complete amino acid sequence of amphiregulin, a bifunctional cell growth modulator, was determined. The truncated form contains 78 amino acids, whereas a larger form of amphiregulin contains six additional amino acids at the amino-terminal end. The amino-terminal half of amphiregulin is extremely hydrophilic and contains unusually high numbers of lysine, arginine, and asparagine residues. The carboxyl-terminal half of amphiregulin (residues 46 to 84) exhibits striking homology to the epidermal growth factor (EGF) family of proteins. Amphiregulin binds to the EGF receptor but not as well as EGF does. Amphiregulin fully supplants the requirement for EGF or transforming growth factor-alpha in murine keratinocyte growth, but it is a much weaker growth stimulator in other cell systems.

8/7/102

06794860 89096860

Proviral insertional activation of c-erbB: differential processing of the protein products arising from two alternate transcripts.

Maihle NJ; Raines MA; Flickinger TW; Kung HJ

Department of Molecular Biology and Microbiology, Case Western Reserve University School of Medicine, Cleveland, Ohio 44106.

Mol Cell Biol Nov 1988, 8 (11) p4868-76, ISSN 0270-7306

Journal Code: NGV

Contract/Grant No.: HD07104-11; CA-39207; P30 CA-43703

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Proviral insertional activation of c-erbB results in the expression of two alternate transcripts (ENV+ and ENV-). We used cDNA clones representing the two alternate transcripts to generate stably transformed quail fibroblast cell lines which express the products of these transcripts independently. Analysis of the co- and posttranslational processing of the insertionally activated c-erbB products expressed in these cell lines revealed that the protein products of the ENV+ and ENV- transcripts were processed differently. The ENV+ transcript produced a primary translation product which was rapidly cotranslationally cleaved near the amino terminus to form a 79,000-Mr product. This protein product was efficiently converted to a higher-molecular-weight form, of between 82,000 and 88,000 (gp82-88), which was terminally glycosylated and expressed on the cell surface. A small portion of the ENV+ primary translation product underwent a second proteolytic cleavage to generate an unglycosylated 53,000-Mr species. In contrast, the primary translation product of the ENV- transcript, 087, was

not proteolytically processed; this precursor form was rapidly converted to two discrete glycosylation intermediates, gp82 and gp84. Only a small portion (less than 10%) of the total ENV- insertionally activated c-erbB product was slowly converted to the terminally glycosylated cell surface form, gp85-88. The processing differences that distinguished the ENV+ and ENV- products were similar to processing differences that we observed in parallel studies on the viral erbB products of the avian erythroblastosis viruses AEV-H and AEV-R, respectively. (ABSTRACT TRUNCATED AT 250 WORDS)

8/7/106

06728600 89030600

Truncation of the human EGF receptor leads to differential transforming potentials in primary avian fibroblasts and erythroblasts.

Khazaie K; Dull TJ; Graf T; Schlessinger J; Ullrich A; Beug H; Vennstrom B

Differentiation Programme, European Molecular Biology Laboratory, Heidelberg, FRG.

EMBO J Oct 1988, 7 (10) p3061-71, ISSN 0261-4189 Journal Code: EMB

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The transforming capacity of the normal and mutant human EGF receptor (EGFR) was investigated in primary chicken cells. In fibroblasts, both N- and C-terminal truncations resulted in a weak, additive oncogenic activity. However, not even double truncations caused a v-erbB-like phenotype. Upon EGF-binding, on the other hand, both normal and C-terminally truncated EGFRs resembled v-erbB in their fibroblast transforming potential. In erythroblasts, N-terminal truncation was sufficient to induce constitutive self-renewal, which was enhanced by deletion of 32 C-terminal amino acids but abolished by a larger truncation of 202 amino acids. In contrast to the normal EGFR, the receptor lacking 32 C-terminal amino acids resembled v-erbB in conferring erythropoietin independence for spontaneous differentiation to the transformed erythroblasts. Our results indicate that the C-terminal domain of the EGFR is non-essential in fibroblast transformation, but seems to be crucial for both self renewal induction and specificity of receptor function in erythroblasts.

8/7/108

06715228 89017228

Properties of the insulin receptor ectodomain.

Johnson JD; Wong ML; Rutter WJ

Hormone Research Institute, University of California, San Francisco 94143.

Proc Natl Acad Sci U S A Oct 1988, 85 (20) p7516-20, ISSN 0027-8424

Journal Code: PV3

Contract/Grant No.: DK37661

Languages: ENGLISH

Document type: JOURNAL ARTICLE

To study the properties of the extracellular insulin-binding domain of the human insulin receptor (hIR), we have expressed portions of the parent molecule in mammalian cells. Receptor cDNAs encoding the entire hIR ectodomain, the alpha subunit of the hIR alone, or a portion of the alpha subunit containing the cysteine-rich region were placed within an expression vector and in turn used to transfect CHO cells. Only cells expressing mRNA for the entire hIR ectodomain secreted hIR-related protein, suggesting that the truncated versions of this domain are unstable. The ectodomain molecules were extensively glycosylated, properly processed heterotetramers. Further, they bound insulin with an affinity similar to that of the intact hIR. In the electron microscope the secreted ectodomains appeared as discrete globular structures. After incubation with roughly equimolar quantities of insulin, the ectodomains associated to form loops or branched and folded linear macroarrays. However, these structures were not restricted to the specific ligand, insulin, since epidermal growth factor also produced the effect. Nevertheless, it seems that the receptor ectodomains can exist in two structural states. The conversion of the singular to the aggregated state may somehow be associated with transmembrane communication and activation of the biological response.

8/7/111

06685708 88330708

Analysis of structure and activation of some receptor-type tyrosine kinase oncogenes.

Shibuya M; Matsushime H; Yamazaki H; Wang LH; Fukui Y; Ueyama Y; Tamaoki N

Institute of Medical Science, University of Tokyo, Japan.

Int Symp Princess Takamatsu Cancer Res Fund 1986, 17 p195-202,

Journal Code: HHI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

We first describe the characterization of proto-oncogene of v-ros in chicken and human genomes. v-ros sequence of UR2 avian sarcoma virus carries a hydrophobic short stretch upstream of the kinase domain, suggesting that its proto-oncogene encodes for a receptor molecule. Using v-ros DNA as a probe we isolated chicken and human c-ros proto-oncogenes. These c-ros DNAs contained a tyrosine kinase domain, transmembrane domain and a part of an extracellular domain carrying an N glycosylation site which was not acquired by UR2 sarcoma virus. These results strongly suggest that proto-oncogene c-ros encodes for a receptor of cell growth or differentiation factor(s) and that the v-ros sequence is a truncated form of this receptor molecule. Structural alteration and overexpression under the control of viral promoter may be crucial for transforming activity of v-ros gene. We then report another example where a receptor-type oncogene is qualitatively and quantitatively activated. By screening with various onc probes we detected two human glioblastomas which have amplification of structurally altered c-erbB1 (epidermal growth factor (EGF) receptor) gene. c-erbB1 gene in these tumors bears a small deletion within the extracellular domain, and the gene product 140 kd protein shorter than the normal 170 kd EGF receptor was heavily phosphorylated on tyrosine residue even without ligand in in vitro phosphorylation reaction. Thus, these mutated EGF receptors seem to be fixed as a "switch-on" form in signal transduction for cell growth and might be involved in the transformation of glial cells.

8/7/112

06685707 88330707

Altered expression of epidermal growth factor receptors in human bladder and lung tumours.

Berger MS; Greenfield C; Waterfield MD

Ludwig Institute for Cancer Research, Middlesex Hospital/University College Branch, London, U.K.

Int Symp Princess Takamatsu Cancer Res Fund 1986, 17 p183-94,

Journal Code: HHI

Languages: ENGLISH

Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL

The expression of epidermal growth factor (EGF) receptors on 31 primary bladder and 109 lung tumours was evaluated by immunohistology using two monoclonal antibodies which recognise either the external ligand binding domain or the internal tyrosine kinase domain. At the immunocytochemical level receptor over-expression was detected at a higher frequency in squamous lung tumours than in other types of lung tumours. In the bladder tumours those with the highest level of EGF receptor expressions were invasive and poorly differentiated. In all tumours similar receptor expression levels were detected with both antibodies indicating that expression of truncated receptors is not detectable by this method. Analysis of DNA from the bladder and lung tumours failure to show gene re-arrangement, except in one unusual case of a carcinosarcoma, thus confirming these histochemical results. Gene amplification accompanied by massive overexpression of receptors was found in 1 of 29 bladder tumours and in 2 of 10 squamous cell carcinomas of the lung. The results suggest that analysis of receptor overexpression could prove useful for diagnosis of certain tumours. (30 Refs.)

8/7/116

06378414 88223414

Biosynthesis of the epidermal growth factor receptor in human squamous cell carcinoma lines: secretion of the truncated receptor is not common to epidermal growth factor receptor-hyperproducing cells.

Gamou S; Hirai M; Rikimaru K; Enomoto S; Shimizu N

Department of Molecular Biology, Keio University School of Medicine, Tokyo, Japan.

Cell Struct Funct Feb 1988, 13 (1) p25-38, ISSN 0386-7196

Journal Code: CSF

Contract/Grant No.: GM24375

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The biosynthesis of the EGF receptor was examined in the epidermoid carcinoma cell line A431 and five novel cell lines from human squamous cell carcinomas possessing high numbers of EGF receptors. Newly synthesized EGF receptors were visualized by labeling with [35S]methionine and immunoprecipitation with a monoclonal anti-EGF receptor antibody. In addition, the processing of the EGF receptor and its intracellular transport was analyzed by distinguishing cell surface receptors from intracellular receptors and by treating cells with inhibitors such as tunicamycin, monensin and brefeldin A. These analyses revealed that in all the tumor cell lines the EGF receptor is synthesized as a glycosylated protein of Mr 160,000 which is converted to the receptor of Mr 170,000 through posttranslational glycosylation. The receptors of Mr 160,000 and 170,000 appeared to possess high mannose type oligosaccharide chains because endoglycosidase H treatment reduced their molecular weights by approximately 30,000. A431 was the only tumor cell line studied that secreted the truncated EGF receptor of Mr 110,000. In A431 cells, the truncated EGF receptor was generated from a protein of Mr 60,000 through tunicamycin- and monensin-sensitive glycosylation. A431 cells treated with monensin secreted the truncated receptor as a Mr 95,000 form.

8/7/120

06432499 88077499

Polypeptide growth factors: roles in normal and abnormal cell growth.

Deuel TF

Department of Medicine and Biological Chemistry, Jewish Hospital at Washington University Medical Center, St. Louis, Missouri 63110.

Annu Rev Cell Biol 1987, 3 p443-92, ISSN 0743-4634 Journal Code:

ARB

Contract/Grant No.: HL31102; HL14147

Languages: ENGLISH

Document type: JOURNAL ARTICLE; REVIEW; REVIEW, ACADEMIC

An increasing number of polypeptide growth factors have been identified that regulate not only cell proliferation but an extraordinary range of cell activities, including matrix protein deposition and resolution, the maintenance of cell viability, cell differentiation, inflammation, and tissue repair. Normal cells appear to require growth factors for proliferation and for maintenance of viability. Cells that secrete a polypeptide growth factor have an advantage in growth. These factors can act either externally through cell surface receptors or perhaps internally during the transport of receptors and growth factors through the ER and Golgi, causing autocrine stimulation of cell growth. Depending on the cell type, growth factors can also be potent inhibitors of cell growth rather than stimulating growth, and the effects can depend on the presence or absence of other growth factors. Platelet-derived growth factor has been shown to be nearly identical to the product of the v-sis gene of the simian sarcoma virus, which appears to cause cell transformation through its interactions with the PDGF receptor activating the tyrosine kinase activity of the PDGF receptor. Similarly, two proto-oncogenes, c-erbB and c-fms, encode growth factor receptors. The EGF receptor activity of the v-erb oncogene product appears to be constitutively activated without the need for growth factor, perhaps because of the truncation at the amino terminus deleting the EGF binding domain. The induction of the myc and the fos proteins by growth factor stimulation of quiescent cells, as well as the potential for the p21 product of the ras oncogene to act as an intermediate

in producing adrenergic signals, provide direct evidence that these pathways are important for stimulation of cell growth. Cells transformed by the v-sis oncogene always appear to bear PDGF cell surface receptors, which suggests that this oncogene has a specific requirement of the PDGF receptor for transformation. In contrast, cells transformed by the v-erbB and v-fms oncogenes are not stimulated by EGF or by CSF-1. Thus it seems likely that the tyrosine kinase activity of the corresponding receptor is ubiquitously expressed in these cases. Major questions remain unanswered. In particular, what are the mechanisms by which growth factors initiate pathways leading to DNA synthesis? What are the physiological substrates of the growth factor receptor tyrosine kinase? Considerable effort also is needed to further define the cellular specificity of the different growth factors, particularly within intact tissues, and to determine how the various growth factors interact. (ABSTRACT TRUNCATED AT 400 WORDS) (434 Refs.)

8/7/122

06278934 87252934

Transmembrane signaling of interleukin 2 receptor. Conformation and function of human interleukin 2 receptor (p55)/insulin receptor chimeric molecules.

Hatakeyama M; Doi T; Kono T; Maruyama M; Minamoto S; Mori H; Kobayashi M; Uchiyama T; Taniguchi T

J Exp Med Aug 1 1987, 166 (2) p362-75, ISSN 0022-1007

Journal Code: I2V

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Chimeric genes were constructed which gave rise to the expression of novel receptor molecules consisting of the extracellular domain of the human interleukin 2 receptor (IL-2-R; p55 or Tac antigen) joined to the transmembrane domain and either full-length or truncated cytoplasmic domain of the human insulin receptor (Ins-R). Expression studies using mouse T cell line EL-4 revealed that the chimeric receptors are able to manifest properties indistinguishable from the authentic IL-2-R. On the other hand, stimulation of the tyrosine kinase activity by IL-2 was not observed in the chimeric receptor with the entire cytoplasmic domain of the Ins-R. These findings thus shed light on the structural conformation and functioning of the IL-2-R complex.

8/7/125

06203984 87177984

A chimeric, ligand-binding v-erbB/EGF receptor retains transforming potential.

Riedel H; Schlessinger J; Ullrich A

Science Apr 10 1987, 236 (4798) p197-200, ISSN 0036-8075

Journal Code: UJ7

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Comparison of amino acid sequences from human epidermal growth factor (EGF) receptor and avian erythroblastosis virus erbB oncogene product suggests that v-erbB represents a truncated avian EGF receptor gene product. Although both proteins are transmembrane tyrosine kinases, the v-erbB protein lacks most of the extracellular ligand-binding domain and a 32-amino acid cytoplasmic sequence present in the human EGF receptor. To test the validity of the proposed origin of v-erbB and to investigate the functional significance of the deleted extracellular sequences, a chimeric gene encoding the extracellular and the transmembrane domain of the human EGF receptor joined to sequences coding for the cytoplasmic domain of the avian erbB oncogene product was constructed. When expressed in Rat1 fibroblasts, this reconstituted gene product (HER-erbB) was transported to the cell surface and bound EGF. Its autophosphorylation activity was stimulated by interaction with the ligand. Expression of the HER-erbB chimera led to anchorage-independent cell growth in soft agar and EGF-induced focus formation in Rat1 monolayers. Thus, it appears that v-erbB protein sequences in the chimeric receptor retain their transforming activity under the influence of the human extracellular EGF-binding domain.



07/17/13

06003479 86304479

Regulation of kinase and intermolecular bonding in intact and truncated epidermal growth factor receptor.

Basu M; Sen-Majumdar A; Basu A; Murthy U; Das M

J Biol Chem Sep 25 1986, 261 (27) p12879-82, ISSN 0021-9258

Journal Code: HIV

Contract/Grant No.: CA-43787; HD-17896

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Tyrosine kinase activity of the epidermal growth factor (EGF) receptor can be regulated by its state of association. Studies done with the purified receptor solubilized in Triton X-100 indicate that dimer formation results in negative regulation of kinase, whereas successive binding of EGF and ATP shift the association equilibrium toward the catalytically active monomeric form. The promotion of the monomeric state by ATP can be mimicked by various nonphosphorylating analogs indicating that nucleotide binding rather than autophosphorylation is responsible for stabilizing the monomeric receptor form. Truncated receptor forms, lacking either the external EGF-binding domain or the internal kinase (ATP-binding) domain, are unable to form stable dimers. These results suggest that both intra- and extracellular domains of the receptor act to stabilize the kinase-regulatory dimer.

8/7/137

05817663 86118663

Similarity of protein encoded by the human c-erb-B-2 gene to epidermal growth factor receptor.

Yamamoto T; Ikawa S; Akiyama T; Semba K; Nomura N; Miyajima N; Saito T; Toyoshima K

Nature Jan 16-22 1986, 319 (6050) p230-4, ISSN 0028-0836

Journal Code: NSC

Languages: ENGLISH

Document type: JOURNAL ARTICLE

A novel v-erb-B-related gene, c-erb-B-2, which has been identified in the human genome, maps to human chromosome 17 at q21 (ref. 40), and seems to encode a polypeptide with a kinase domain that is highly homologous with, but distinct from, that of the epidermal growth factor (EGF) receptor. The c-erb-B-2 gene is conserved in vertebrates and it has been suggested that the neu gene, detected in a series of rat neuro/glioblastomas, is, in fact, the rat c-erb-B-2 gene. Amplification of the c-erb-B-2 gene in a salivary adenocarcinoma and a gastric cancer cell line MKN-7 suggests that its over-expression is sometimes involved in the neoplastic process. To determine the nature of the c-erb-B-2 protein, we have now molecularly cloned complementary DNA for c-erb-B-2 messenger RNA prepared from MKN-7 cells. Its sequence shows that the c-erb-B-2 gene encodes a possible receptor protein and allows an analysis of the similarity of the protein to the EGF receptor and the neu product. As a consequence of chromosomal aberration in MKN-7 cells, a 4.6-kilobase (kb) normal transcript and a truncated 2.3-kb transcript of c-erb-B-2 are synthesized at elevated levels. The latter transcript presumably encodes only the extracellular domain of the putative receptor.

?t s10/7/17-21 25

10/7/17

07637700 91156700

Native avian c-erbB gene expresses a secreted protein product corresponding to the ligand-binding domain of the receptor.

Maihle NJ; Flickinger TW; Raines MA; Sanders ML; Kung HJ

Department of Biochemistry and Molecular Biology, Mayo Clinic and Foundation, Rochester, MN 55905.

Proc Natl Acad Sci U S A Mar 1 1991, 88 (5) p1825-9, ISSN 0027-8424

Journal Code: PV3

Contract/Grant No.: CA 51197, CA, NCI; CA 39207, CA, NCI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

primer-directed cDNA library was used to obtain cDNA clones corresponding to the 5' end (i.e., the ligand-binding domain) of the avian c-erbB gene. Bacterial c-erbB fusion proteins were synthesized and used to obtain polyclonal antisera specific for the ligand-binding domain of the avian receptor. These antisera and antisera specific for the carboxyl terminal domain of the chicken c-erbB gene product have been used to study the native protein products of the c-erbB locus in primary cell cultures by in vivo labeling and immunoprecipitation. Our studies reveal that three c-erbB gene products of Mr 300,000, Mr 170,000, and Mr 95,000 are synthesized in uninfected chicken embryo fibroblasts. Only the Mr 300,000 and Mr 170,000 species can be precipitated by using antisera specific for the cytoplasmic domain of the c-erbB product. The 95,000 species is not recognized by the antiserum directed against the carboxyl-terminal domain of c-erbB and is specifically released into the culture medium. Northern transfer studies reveal a lower molecular weight transcript of approximately 2.6 kilobases that selectively hybridizes to the ligand-binding domain of the avian c-erbB gene product but does not hybridize with probes specific for the cytoplasmic kinase domain of c-erbB. An additional cDNA clone corresponding to this transcript has been isolated, and its sequence suggests it may arise via alternative processing. Together, these data suggest that a truncated form of this growth factor receptor--i.e., a Mr 95,000 species--is synthesized from a low molecular weight c-erbB transcript that exclusively encodes the ligand-binding domain of the receptor. Secretion of truncated growth factor receptors has been reported recently in several systems, and our results are discussed in the light of these findings.

10/7/18

07423671 90330671

Deletion analysis of the human insulin receptor ectodomain reveals independently folded soluble subdomains and insulin binding by a monomeric alpha-subunit.

Schaefer EM; Siddle K; Ellis L

Howard Hughes Medical Institute, University of Texas Southwestern Medical Center, Dallas 75235-9050.

J Biol Chem Aug 5 1990, 265 (22) p13248-53, ISSN 0021-9258

Journal Code: HIV

Languages: ENGLISH

Document type: JOURNAL ARTICLE

A series of 13 deletions within the extracellular domain of the human insulin receptor delineates the boundaries of subdomains that fold de novo into stable proteins that are efficiently secreted and retain the epitopes required for interaction with two conformation-specific monoclonal antibodies. While most of these proteins fail to bind insulin, a truncation that includes only the alpha-subunit is secreted as a monomer that binds the hormone with an affinity only slightly less than that of the complete heterotetrameric extracellular domain. These results thus demarcate landmarks within the primary sequence which will now guide further analysis of the structure and function of this complex domain of the receptor.

10/7/19

07423649 90330649

Baculovirus-directed expression of the human insulin receptor and an insulin-binding ectodomain [published erratum appears in J Biol Chem 1990 Nov 15;265(32):20051]

Paul JI; Tavaré J; Denton RM; Steiner DF

Howard Hughes Medical Institute, University of Chicago, Illinois 60637.

J Biol Chem Aug 5 1990, 265 (22) p13074-83, ISSN 0021-9258

Journal Code: HIV

Contract/Grant No.: DK 13914, DK, NIDDK

Languages: ENGLISH

Document type: JOURNAL ARTICLE

In this report we describe the use of the baculovirus expression system to overproduce the human insulin holoreceptor (HIR) and a truncated, secretory version of the HIR cDNA (HIRsec) consisting of the alpha subunit and the extracellular portion of the beta subunit (beta'). Sf9 cells

infected with the full-length HIR viruses synthesize recombinant HIR (rHIR) with an insulin-binding alpha subunit of apparent Mr = 110,000 and a beta subunit of apparent Mr = 80,000. Uncleaved alpha beta proreceptor accumulates in infected cells. Both of these forms assemble into higher order disulfide-linked dimers or heterotetramers of apparent Mr greater than 350,000. Insulin-binding activity in cells infected with rHIR viruses is present predominantly on the extracellular aspect of the plasma membrane (greater than 80%). Insulin binding to the full-length rHIR occurs with typical complex kinetics with  $K_{d1} = 0.5-1 \times 10^{-9}$  M and  $K_{d2} = 10^{-7}$  M and receptors are present in large amounts in infected cells ( $1 \times 10^6$  receptors/cell; 1-2 mg HIR/ $10^9$  cells). The full-length rHIR undergoes insulin-dependent autophosphorylation; half-maximal activation of beta subunit autophosphorylation occurs at  $1-2 \times 10^{-8}$  M. The alpha beta proreceptor also becomes phosphorylated in vitro. Analysis of tryptic phosphopeptides derived from in vitro autophosphorylated beta subunit and alpha beta proreceptor reveals a pattern of phosphorylation that is indistinguishable from that of authentic placental HIR. Sf9 cells infected with rHIRsec viruses synthesize and secrete an (alpha beta')<sub>2</sub> heterotetrameric complex having an insulin-binding alpha subunit of apparent Mr = 110,000 and a truncated beta' subunit of apparent Mr = 45,000 that lacks kinase activity. The rHIRsec complex purified from the conditioned medium of infected cells binds insulin with high affinity ( $K_d = 10^{-9}$  M).

10/7/20

07351888 90258888

A truncated, secreted form of the epidermal growth factor receptor is encoded by an alternatively spliced transcript in normal rat tissue.

Petch LA; Harris J; Raymond VW; Blasband A; Lee DC; Earp HS

Department of Pharmacology, University of North Carolina 27599.

Mol Cell Biol Jun 1990; 10 (6) p2973-82, ISSN 0270-7306

Journal Code: NGY

Contract/Grant No.: DK-30002, DK, NIDDK; CA-43793, CA, NCI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Two independent cDNA clones corresponding to a 2.7-kilobase (kb) epidermal growth factor receptor (EGF-R) mRNA were isolated from a rat liver cDNA library. Sequence analysis revealed 100% homology in the external domain when compared with the full-length rat EGF-R nucleotide sequence and 80 to 90% similarity relative to the human EGF-R. However, the 3'-terminal sequence of these clones did not match EGF-R or any other known sequence(s) and was distinct from the 3' end of the 2.8-kb mRNA, which encodes a truncated EGF-R in A431 cells. The deduced amino acid sequence revealed an open reading frame which is homologous to the external domain of the EGF-R but which terminates prior to the transmembrane region. Southern blot analysis of rat genomic DNA indicated that the 3'-terminal sequence of this transcript is derived from the EGF-R gene. Analysis of a genomic clone containing the 3' end of the 2.7-kb transcript revealed that this sequence is present as a discrete exon in the mid-region of the receptor gene in proximity to the exon encoding the transmembrane domain. Introduction of an expression vector containing the truncated EGF-R cDNA into Chinese hamster ovary (CHO) cells led to the expression of a 95-kilodalton protein which was detected in conditioned media, by using antisera directed against the EGF-R. A similarly sized protein was also detected in the media of WB cells, a continuous, nontransformed line of rat hepatic epithelial cells. Northern (RNA blot) analysis established that the truncated receptor is encoded by a 2.7-kb transcript found in normal rat liver. Furthermore, Northern analysis of rat poly(A)+ RNA showed that the 2.7-kb EGF-R transcript is expressed at differing levels in various fetal and adult tissues. These data indicate that alternative splicing of the EGF-R primary transcript yields a 2.7-kb mRNA which codes for a truncated form of the receptor. This receptor is secreted by rat hepatic epithelial cells in culture, which suggests that it may be secreted by normal rat cells or tissues and perhaps serve an as yet unknown physiological function.

07327495 90234495

Truncation of the ectodomain of the human insulin receptor results in secretion of a soluble insulin binding protein from transfected CHO cells.

Ellis L; Sissom J; Levitan A

Howard Hughes Medical Institute, Dallas, TX.

J Mol Recognit Feb 1988, 1 (1) p25-31, ISSN 0952-3499

Journal Code: A00

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The insulin receptor is an integral transmembrane glycoprotein comprised of two alpha-(approximately 135 kDa) and two beta-(approximately 95 kDa) subunits, which is synthesized as a single polypeptide chain precursor (alpha beta). The primary sequence of the human insulin receptor (hIR) protein, deduced from the nucleotide sequence of cloned human placental mRNAs, predicts two large domains (929 and 403 residues) on either side of a single membrane spanning domain (23 residues); each of these major domains has a distinct function (insulin binding and protein/tyrosine kinase activity, respectively). To experimentally test this deduced topology, and to explore the potential for independent domain function by the hIR extracellular domain, we have constructed an expression plasmid encoding an hIR deletion mutant which is truncated 8 residues from the beginning of the predicted transmembrane domain (i.e., 921 residues). This domain of the hIR is in fact processed into alpha- and truncated beta-subunits and secreted with high efficiency from transfected CHO cell lines which express this mutant hIR, and the protein accumulates as an (alpha beta)<sub>2</sub> dimer in the medium. This molecule is recognized by a battery of 13 monoclonal antibodies to epitopes on the IR extracellular domain, four of which block insulin binding and two of which require the native conformation of the IR for recognition. Further, this domain binds insulin with an apparent dissociation constant comparable to that of the wild-type hIR. However, the secreted dimer displays a linear Scatchard plot, while that of the wild-type membrane-associated hIR is curvilinear. (ABSTRACT TRUNCATED AT 250 WORDS)

10/7/25

07072077 89374077

Secretion of the extracellular domain of the human insulin receptor from insect cells by use of a baculovirus vector.

Sissom J; Ellis L

Howard Hughes Medical Institute, Dallas, TX.

Biochem J Jul 1 1989, 261 (1) p119-26, ISSN 0264-6021

Journal Code: 9Y0

Languages: ENGLISH

Document type: JOURNAL ARTICLE

To explore the utility of the baculovirus/insect-cell system for the expression of a soluble secreted human insulin-receptor (hIR) extracellular ligand-binding domain, we have engineered a recombinant virus encoding an hIR deletion mutant which is truncated eight residues from the beginning of the predicted transmembrane domain (i.e. 921 residues). Within 24 h after infection of Sf9 cells with virus, insulin-binding activity begins to accumulate in the culture medium, and reaches a maximum between 48 and 72 h. The intracellular transit and processing of this secreted receptor, designated 'AChIR01', is quite slow. After 24 h in pulse-chase experiments approximately 50% of the metabolically labelled protein is still inside the cell. This protein accumulates as a non-cleaved hIR precursor which is glycosylated, but the carbohydrate is entirely endoglycosidase H (endoH)-sensitive (i.e. high mannose). Approximately one-half of the receptor in the culture medium (i.e. approximately 25% of the total) is in the form of non-cleaved precursor, and about one half of its carbohydrate chains are now endoH-resistant. The remainder of the protein is proteolytically processed hIR (alpha-plus truncated beta-subunits). None of these hIR species exhibit O-linked carbohydrate. Only the processed form of the receptor in the medium binds insulin. This insulin-binding protein is secreted as a dimer (alpha beta)<sub>2</sub>, and binds insulin with an affinity which is comparable with that of both the wild-type hIR as well as the secreted

form or the n/r expressed in mammalian cells. Despite the rather inefficient processing and altered glycosylation of the AchIR01 protein in insect cells, this high-affinity insulin-binding protein accumulates in the medium at levels (mg/litre) of about 100 times that achieved in a mammalian-cell system.

?t s12/7/13

12/7/13

06686114 88331114

Cell surface expression of glycosylated, nonglycosylated, and truncated forms of a cytoplasmic protein pyruvate kinase.

Hiebert SW; Lamb RA

Department of Biochemistry, Molecular Biology and Cell Biology, Northwestern University, Evanston, Illinois 60208.

J Cell Biol Sep 1988, 107 (3) p865-76, ISSN 0021-9525

Journal Code: HMV

Contract/Grant No.: AI-20201; AI-23173

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The soluble cytoplasmic protein pyruvate kinase (PK) has been expressed at the cell surface in a membrane-anchored form (APK). The hybrid protein contains the NH<sub>2</sub>-terminal signal/anchor domain of a class II integral membrane protein (hemagglutinin/neuraminidase, of the paramyxovirus SV5) fused to the PK NH<sub>2</sub> terminus. APK contains a cryptic site that is used for N-linked glycosylation but elimination of this site by site-specific mutagenesis does not prevent cell surface localization. Truncated forms of the APK molecule, with up to 80% of the PK region of APK removed, can also be expressed at the cell surface. These data suggest that neither the complete PK molecule nor its glycosylation are necessary for intracellular transport of PK to the cell surface, and it is possible that specific signals may not be needed in the ectodomain of this hybrid protein to specify cell surface localization.

?b 351;exs

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\$2.74 0.083 Hrs File155

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\$5.50 Estimated cost File155

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\$6.50 Estimated total session cost 0.083 Hrs.

File 351:DERWENT WORLD PATENTS INDEX-LATEST

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Set	Items	Description
S1	52	HER2 OR NEU OR P185 OR C(W)ERBB
S2	28	INSULIN(W)RECEPTOR OR (IGF OR INSULIN(W)LIKE(W)GROWTH(W)FA- CTOR)(W)RECEPTOR
S3	43	(EGF OR EPIDERMAL(W)GROWTH(W)FACTOR)(W)RECEPTOR
S4	115	S1 OR S2 OR S3
S5	11757	TRUNCAT?
S6	2	S4 AND S5
S7	754464	EXTRACELLULAR OR EXTERNAL OR SURFACE OR LIGAND(W)BINDING OR HYDROPHILIC OR (AMINO OR N)(W)TERMINAL
S8	1	S6 AND S7
S9	5981	SECRET?
S10	0	S8 AND S9
S11	2	ECTODOMAIN
S12	0	S5 AND S11 NOT S8

?t s6/7/1-2

6/7/1

009502761 WPI Acc No: 93-196297/24

XRAM Acc No: C93-087034

New epidermal growth factor receptor truncate proteins - which bind ligands of EGF receptor without transmitting signal for growth or reproduction

Patent Assignee: (WARN ) WARNER LAMBERT CO

Author (Inventor): CONNORS R W

Number of Patents: 001

Number of Countries: 001

Patent Family:

CC Number	Kind	Date	Week	
US 5218090	A	930608	9324	(Basic)

Priority Data (CC No Date): US 536896 (900612); US 604728 (901026)

Abstract (Basic): US 5218090 A

An epidermal growth factor (EGF) receptor truncate protein selected from LD1D2D3 ApaL, LD2D3D4 and LD3D4 having EGD binding sites is claimed.

USE/ADVANTAGE - The truncate proteins bind ligands of the EGF receptor without transmitting a signal for the growth and reproduction of a cell. They can be used as absorptive agents for any moieties that bind the EGF receptor such as EGF and TGF-alpha and viruses that use the EGF receptor as the portal of entry to a cell. The proteins will compete with the EGF receptor present on the cell surface for binding of the ligands and thereby inhibit the action of the ligands or prevent entry of viruses into cells. The proteins can also be used as for the EGF receptor itself, such as in the detection of abnormalities in mammalian cell growth. The proteins are also useful for prepg. novel

receptors for efficient detn. of ligands and their antagonists or agonists. Dwg.0/12  
Derwent Class: B04; D16;  
Int Pat Class: C07K-013/00; C12N-015/12

6/7/2

004369735 WPI Acc No: 85-196613/32

XRAM Acc No: C85-085921

XRPX Acc No: N85-147490

Diagnosis of neoplastic and related diseases by assay of human test sample for altered or abnormally expressed growth factor receptors or for M-RNA transcripts of genes encoding them

Patent Assignee: (ICRF-) ICRF PATENTS LTD; (YEDA ) YEDA RES & DEV CO LTD; (GETH ) GENENTECH INC; (WATE/) WATERFIELD M D

Author (Inventor): SCHLESSINGER J; ULLRICH A; WATERFIELD M D; SCHLESSING J; WATERFIELD M

Number of Patents: 006

Number of Countries: 013

Patent Family:

CC Number	Kind	Date	Week	
WO 8503357	A	850801	8532	(Basic)
AU 8539340	A	850809	8543	
EP 171407	A	860219	8608	
JP 61501168	W	860612	8630	
US 4933294	A	900612	9031	
EP 491675	A1	920624	9226	

Priority Data (CC No Date): GB 842379 (840130); GB 85538 (850109)

Applications (CC,No,Date): EP 92101700 (850130); WO 85GB45 (850130); EP 85900716 (850130); JP 85500645 (850130); US 783951 (851202)

Language: English

EP and/or WO Cited Patents: No-citns.; 11Jnl.Ref; 10Jnl.Ref

Designated States

(National): AU; JP; US

(Regional): AT; BE; CH; DE; FR; GB; LI; LU; NL; SE

Filing Details: EP0491675 Related to EP 171407

Abstract (Basic): WO 8503357

(1) Antibody capable of binding a predetermined aminoacid sequence within the epidermal growth factor (EGF) receptor is new. (2) Antigenic analogue comprising an immunogenic polymer bound to a polypeptide fragment of the EGF receptor is new. (3) DNA or RNA encoding the EGF receptor or a fragment of it is new. (4) DNA or RNA capable of hybridising with DNA or RNA encoding the EGF receptor or a fragment of it is new. (5) Diagnostic procedure comprises obtg. a test sample from a human and assaying it for structurally altered or abnormally expressed growth factor receptors, or for the mRNA transcripts or genes encoding them.

USE/ADVANTAGE - The diagnostic test with body fluids, tissues, etc. is carried out at the protein, RNA, or DNA level. Structural alterations of human EGF receptor and its gene, or in transcription and expression of the gene can be involved in tumourgenesis. The assays are therefore useful in the deternn. and control of tumours in humans. The antibodies etc. are used in the diagnostic test. The antigenic analogues are useful in drug targetting and with the polypeptide fragments, may be used to inhibit the activity of normal or abnormal ECF receptors expressed in cancer cells. The polypeptides provide a basis for construction of synthetic oligonucleotides encoding them.

@(72pp Dwg.No.0/8)@

Abstract (US): 9031 US 4933294

Diagnosis for the detection of abnormalities in mammalian cell growth comprises obtg. a test sample from a human and assaying the sample of a truncated epidermal growth factor receptor having at least a portion of its mature amino terminus deleted, and correlating detection of the truncated growth factor receptor with abnormal growth control in mammalian cells.

USE/ADVANTAGE - Neoplastic and other diseases can be diagnosed by

assaying e.g. body fluid, tissue or cultured tumour explant cells for structurally altered or abnormally expressed growth factor receptors. @ (25pp) @

Derwent Class: B04; C03; D16; S03; R16;

Int Pat Class: A61K-039/39; A61K-039/395; A61K-049/00; C07K-007/04; C07K-015/00; C12P-021/00; C12Q-001/68; G01N-033/57; G01N-033/574

?s s4 and s7

115 S4  
754464 S7

S13 24 S4 AND S7

t s13/7/8 12 18 19 24

13/7/8

009072174 WPI Acc No: 92-199589/24

Related WPI Accession(s): 92-123385; 93-188588; 93-226664

XRAM Acc No: C92-090853

Nucleic acid encoding polypeptide fusions - comprising ligand binding partner protein and immunoglobulin chain, for use in diagnosis and therapy

Patent Assignee: (GETH ) GENENTECH INC

Author (Inventor): CAPON D J; LASKY L A

Number of Patents: 001

Number of Countries: 001

Patent Family:

CC Number	Kind	Date	Week	
US 5116964	A	920526	9224	(Basic)

Priority Data (CC No Date): US 315015 (890223); US 440625 (891122)

Abstract (Basic): US 5116964 A

The following are claimed: (A) nucleic acid encoding a polypeptide fusion comprising a ligand binding partner protein (LBPP) contg. more than one polypeptide chain, where LBPP is not a platelet growth factor receptor or an insulin receptor, one of the chains being fused to an immunoglobulin constant region through C- or N-terminal amino or carboxyl gps.; (B) nucleic acid encoding a polypeptide fusion of a LBPP and an immunoglobulin chain, where the LBPP is not a platelet growth factor receptor or an insulin receptor, the LBPP and the immunoglobulin chain being fused through C- or N-terminal amino or carboxyl gps., and the fusion further comprising an additional fusion of an agent selected from a multiple subunit (chain) polypeptide, a portion of an immunoglobulin superfamily member, a toxin and a polypeptide therapeutic agent not otherwise associated with an immunoglobulin, and an immunoglobulin chain; (C) nucleic acid encoding a polypeptide fusion comprising a LBPP which comprises a lymphocyte cell surface glycoprotein (LHR) and an immunoglobulin chain, in which the LBPP and immunoglobulin are fused through C- or N-terminal amino or carboxyl gps..

USE - The fusion of the immunoglobulin chain to the LBPP prolongs the in vivo plasma half-life of the LBPP and facilitates its purification. The polypeptide fusions combine the adhesive and targeting characteristics of the LBPP with immunoglobulin effector functions such as complement binding and cell receptor binding. They can be used therapeutically or as diagnostic reagents for the in vitro assay of LBPPs or their targets. In particular, the LHR-immunoglobulin hybrid is used therapeutically to compete with the normal binding of lymphocyte to lymphoid tissue. The hybrid is therefore useful for organ or graft rejection, for treatment of inflammation, e.g. due to rheumatoid arthritis or other autoimmune diseases, for control of lymphoma metastasis, in treating conditions in which there is an accumulation of lymphocytes and for targeting therapeutic moieties to lymphoid tissues, eg. for treating tissues infected with viruses such as HIV Dwg. 0/10

Derwent Class: B04; D16;

Int Pat Class: C07H-021/04; C12N-015/62; C12P-021/02



13/7/18  
008849755 WPI Acc No: 91-353773/48

XRAM Acc No: C91-152614

XRPX Acc No: N91-270909

- New hybrid cellular receptor - has 2 sequences encoding extracellular domain of receptors having different ligand binding specificity e.g. insulin- and IGF-receptors

Patent Assignee: (NOVO ) NOVO-NORDISK AS; (NOVO ) NOVO NORDISK A/S

Author (Inventor): ANDERSEN A; KJELDSSEN T; MOELLER N P; RASMUSSEN J; WIBERG F; ANDERSEN A S; KJELDSSEN T B; MOELLER N P H; RASMUSSEN J S; WIBERG F C; KJELDSSEN T; MOLLER N

Number of Patents: 004

Number of Countries: 026

Patent Family:

CC Number	Kind	Date	Week	
WO 9117252	A	911114	9148	(Basic)
AU 9177921	A	911127	9210	
FI 9204890	A	921028	9304	
EP 528878	A1	930303	9309	

Priority Data (CC No Date): DK 901063 (900430); DK 901855 (900803)

Applications (CC,No,Date): EP 91909103 (910430); WO 91DK115 (910430); WO 91DK115 (910430); FI 924890 (921028)

Language: English

EP and/or WO Cited Patents: 3.Jnl.Ref; EP 325262

Designated States

(National): AU; BG; CA; FI; HU; JP; KR; NO; PL; RO; SU; US

(Regional): AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE

Filing Details: EP0528878 Based on WO 9117252

Abstract (Basic): WO 9117252

A hybrid DNA construct (I), comprising a 1st sequence (Ia) encoding part of the extracellular domain of a 1st cellular receptor and a 2nd sequence (Ib) encoding part of the extracellular domain of a 2nd cellular receptor is new. The two receptors are specific for different ligands.

Also claimed are (1) a hybrid polypeptide (A) encoded by (I), (2) a recombinant expression vector comprising (I), (3) a cell contg. the vector of (2), (4) a process for producing (A) comprising culturing the cell of (3) in a suitable nutrient medium under conditions conducive to expression of (A) and recovering (A) from the culture, (5) a method for identifying the ligand-binding site on a cellular receptor utilising (A), incubated with ligands specific for the receptors, with binding between both detected, and (6) a polypeptide fragment of the extracellular domain of a cellular receptor.

Pref. the sequence of (A) which is a hybrid insulin/insulin-like growth Factor-I (IGF-I) receptor is given in the specification in addn. to the CDNA sequence encoding it.

USE - (A) is useful for screening for ligands or functional equivalents (claimed method) as well as for localising ligand-binding sites. It is also useful for establishing the 3-D structure of the ligand-binding site and designing an analogue or functional equivalent.

@(97pp Dwg.No.0/7)@

Derwent Class: B04; D16; S03;

Int Pat Class: C12N-005/00; C12N-015/62; G01N-033/53

13/7/18

008569503 WPI Acc No: 91-073538/10

XRAM Acc No: C91-031175

XRPX Acc No: N91-056832

C-erbB-2 external domain gps. proteins, antibodies, etc. - for use in vaccines, diagnosis and treatment of neoplastic disease

Patent Assignee: (TRIT-) TRITON BIOSCIENCES INC; (TRIT-) TRITON BIOSCI INC

Author (Inventor): STUART S G; MONAHAN J J; LANGTON B C; HANCOCK M E; CHAO L A; BLUFORD P

Number of Patents: 004

Number of Countries: 016

Patent Family:

CC Number	Kind	Date	Week	
WO 9102062	A	910221	9110	(Basic)
AU 9064135	A	910311	9123	
EP 444181	A	910904	9136	
JP 4503012	W	920604	9229	

Priority Data (CC No Date): US 389920 (890804)

Applications (CC,No,Date): JP 90513165 (900802); WO 90US4340 (900802); EP 90914094 (900802)

Language: English

EP and/or WO Cited Patents: NoSR.Pub

Designated States

(National): AU; CA; JP

(Regional): AT; BE; CH; DE; DK; ES; FR; GB; IT; LU; NL; SE; LI

Filing Details: JP04503012 Based on WO 9102062

Abstract (Basic): WO 9102062

The following are claimed:- (1) A recombinant DNA molecule coding for the external domain of the c-erbB-2 protein (gp.75) or its fragment linked to an expression control sequence. (2) A prokaryotic or eukaryotic host cell transformed with the DNA. Cells include: E. coli, Pseudomonas, Bacillus, yeast, other fungi, animal, insect and plant cells. (3) Recombinant gp. 75 proteins which are glycosylated and serologically active; and their production by transforming a unicellular host with recombinant DNA. (4) Monoclonal and polyclonal antibodies to the proteins which may be used in treatment of neoplastic disease. (5) A method of testing mammalian body fluids for presence of gp. 75 especially for detection of breast adenocarcinoma or ovarian adenocarcinoma, and (6) A vaccine comprising substantially pure gp. 75 proteins or cell membranes containing the proteins to immunise a human against neoplastic disease.

USE/ADVANTAGE - For detection of the external domain of c-erbB-2 and gp.75 in diagnosis of neoplastic disease. Also for prophylaxis and treatment of tumours that express the c-erbB-2 oncogene. @ (91pp Dwg.No.0/15)@

Derwent Class: B04; D16; R16;

Int Pat Class: A61K-033/24; A61K-037/02; A61K-039/00; C07K-013/00; C07K-015/00; C12N-001/19; C12N-005/10; C12N-009/12; C12N-015/12; C12P-021/08; G01N-033/53; G01N-035/53

13/7/19

008488946 WPI Acc No: 90-375946/50

XRAM Acc No: C90-163774

HER2 extracellular domain used as vaccine - comprises sequence of at least 9 aminoacid(s) prep'd. using expression vector of DNA isolated from human epidermal growth factor receptor

Patent Assignee: (GETH ) GENENTECH INC

Author (Inventor): HUDZIAK R M; SHEPARD H M; ULLRICH A

Number of Patents: 002

Patent Family:

CC Number	Kind	Date	Week	
WO 9014357	A	901129	9050	(Basic)
EP 474727	A	920318	9212	

Priority Data (CC No Date): US 354319 (890519)

Applications (CC,No,Date): WO 90US2697 (900518); EP 90908809 (900518)

Language: English

EP and/or WO Cited Patents: US 4761371; S.Jnl.REF

Designated States

(National): CA

(Regional): AT; BE; CH; DE; DK; ES; FR; GB; IT; LU; NL; SE; LI

Filing Details: EP0474727 Based on WO9014357 (PT)

Abstract (Basic): WO 9014357

An extracellular portion of HER2 molecule comprises at least 9 amino acids and is an immune epitope, which is at least 99% pure being free of transmembrane and intracellular portions of HER2 molecule. The extracellular portion is antigenic in animals and is conjugated with a

peptide having immunogenic properties. Preparation of extracellular portion comprises ligating a DNA isolate of at least 9 amino acids terminated upstream of the portion encoding the transmembrane or intracellular portions of the HER2 molecule, into an expression vector to transform a suitable host which when cultured under suitable conditions gives rise to the extracellular portion.

USE/ADVANTAGE - Preparing vaccines from the extracellular domains of host cell. @ (48pp Dwg.No.0/13)@

Derwent Class: B04; D16;

Int Pat Class: C07K-007/06; C07K-013/00; C07K-017/00; C12N-001/19; C12N-005/10; C12N-015/12; A61K-039/00; C12P-021/02

13/7/24

007820435 WPI Acc No: 89-085547/11

XRAM Acc No: C89-037987

Recombinant pox virus expressing tumour-associated antigen - used as vaccines against tumour cells and for producing antibodies for immunotherapy or diagnosis

Patent Assignee: (BIOT-) APPL BIOTECHN INC; (WHIT-) WHITEHEAD INST BIOMED RES

Author (Inventor): PANICALI D L; BERNARDS R

Number of Patents: 001

Patent Family:

CC Number	Kind	Date	Week
WO 8901973	A	890309	8911 (Basic)

Priority Data (CC No Date): US 92036 (870902)

Applications (CC,No,Date): WO 88US3032 (880901)

Language: English

EP and/or WO Cited Patents: No.SR.Pub; GB 2188637; 8.Jnl.REF

Designated States

(National): JP

(Regional): AT; BE; CH; DE; FR; GB; IT; LU; NL; SE

Abstract (Basic): WO 8901973

A recombinant pox virus capable of expressing in a host a cell-encoded, tumour-associated antigen is claimed. The pox virus is pref. a vaccinia virus. The tumour antigen may be encoded by the neu gene, the ros gene, the trk gene, the kit gene or a portion of these or the antigen may be a growth factor receptor or growth factor receptor-like cell surface molecule.

USE/ADVANTAGE - The live recombinant viruses can be used to induce an immune response, both humoral and cell-mediated, against tumour cells which express the protein. They can also be used to produce antibody against the antigen for use in therapeutics or diagnostics. The antibodies may be useful in passive immunotherapy against tumour. They may also be used to quantify the antigen in a biological fluid. Cells infected in vitro with the recombinant pox viruses can be used as a source of tumour associated antigens. @ (46pp Dwg.No.0/4)@

Derwent Class: B04; D16;

Int Pat Class: A61K-039/00; C12N-015/00

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\$15.93 Estimated total session cost 0.033 Hrs.

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3/3/112 (Item 2 from file: 399)

119087204 CA: 119(9)87204s JOURNAL

Real-time measurements of kinetics of EGF binding to, soluble EGF receptor monomers and dimers support the dimerization model for receptor activation

AUTHOR(S): Zhou, M.; Felder, S.; Rubinstein, M.; Huz witz, D. R.; Ullrich, A.; Lax, I.; Schlessinger, J.

LOCATION: Med. Cent., New York Univ., New York, NY, 10016, USA

JOURNAL: Biochemistry DATE: 1993 VOLUME: 32 NUMBER: 32 PAGES: 8193-8

CODEN: BICHAW ISSN: 0006-2960 LANGUAGE: English

Copyright 1993 by the American Chemical Society

3/3/113 (Item 3 from file: 399)

112176923 CA: 112(19)176923y PATENT

Monoclonal antibodies against the HER2 receptor, and their use in treating tumor cells

INVENTOR(AUTHOR): Hudziak, Robert M.; Shepard, H. Michael; Ullrich, Axel

LOCATION: USA

ASSIGNEE: Genentech, Inc.

PATENT: PCT International ; WO 8906692 A1 DATE: 890727

APPLICATION: WO 89US51 (890105) \*US 143912 (880112) \*US 147461 (880125)

PAGES: 52 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C12P-021/00A; C12N-015/00B; C12N-005/00B; G01N-033/574B; A61K-039/395B

DESIGNATED COUNTRIES: JP

Copyright 1993 by the American Chemical Society

3/3/114 (Item 1 from file: 351)

009174662 WPI Acc No: 92-302096/37

XRAM Acc No: C92-134631

XRPX Acc No: N92-231094

Recombinant antibodies directed to growth factor receptor C-ERBB-2 - for diagnosing and treating tumours expressing C-ERBB-2 e.g. breast or ovarian tumours

Patent Assignee: (CIBA ) CIBA GEIGY AG

Author (Inventor): GRONER B; HARDMAN N; HARWERTH I; HYNES N E; WELS W S; ZWICKL M

Patent Family:

CC Number	Kind	Date	Week
EP 502012	A1	920909	9237 (Basic)
AU 9210421	A	920813	9240
CA 2060544	A	920806	9243

Priority Data (CC No Date): EP 91810079 (910205)

Applications (CC,No,Date): EP 92810056 (920127); AU 9210421 (920123); CA 2060544 (920203)

3/3/115 (Item 2 from file: 351)

008488946 WPI Acc No: 90-375946/50

XRAM Acc No: C90-163774

HER2 extracellular domain used as vaccine - comprises sequence of at least 9 aminoacid(s) prep'd. using expression vector of DNA isolated from human epidermal growth factor receptor

Patent Assignee: (GETH ) GENENTECH INC

Author (Inventor): HUDZIAK R M; SHEPARD H M; ULLRICH A

Patent Family:

CC Number	Kind	Date	Week
WO 9014357	A	901129	9050 (Basic)
EP 474727	A	920318	9212

Priority Data (CC No Date): US 354319 (890519)

Applications (CC,No,Date): WO 90US2697 (900518); EP 90908809 (900518)

3/3/116 (Item 3 from file: 351)

007968734 WPI Acc No: 89-23384 32

XRAM Acc No: C89-104136

3/3/106 (Item 18 from file: 5)

6475909 BIOSIS Number: 8501130

RELEASE OF TISSUE-TYPE PLASMINOGEN ACTIVATOR IS INDUCED IN RATS BY  
LEUKOTRIENES C-4 AND D-4 BUT NOT BY PROSTAGLANDINS E-1 E-2 AND I-2

TRANQUILLE N; EMEIS J J

GAUBIUS INST. TNO, HERENSTR. 5D, 2313 AD LEIDEN, NETH.

BR J PHARMACOL 93 (1). 1988. 156-164. CODEN: BJPCB

Full Journal Title: British Journal of Pharmacology

Language: ENGLISH

3/3/107 (Item 19 from file: 5)

5889729 BIOSIS Number: 84022294

GRAY PLATELET SYNDROME STUDIES ON PLATELET ALPHA-GRANULES LYSOSOMES AND  
DEFECTIVE RESPONSE TO THROMBIN

SRIVASTAVA P C; POWLING M J; NOKES T J C; PATRICK A D; DAWES J; HARDISTY  
R M

DEP. HAEMATOL./ONCOL., HOSP. SICK CHILDREN, GREAT ORMOND ST., LONDON WC1N  
3JH.

BR J HAEMATOL 65 (4). 1987. 441-446. CODEN: BJHEA

Full Journal Title: British Journal of Haematology

Language: ENGLISH

3/3/108 (Item 20 from file: 5)

5884122 BIOSIS Number: 84016687

A CHIMERIC LIGAND-BINDING V-ERB-B-EGF RECEPTOR RETAINS TRANSFORMING  
POTENTIAL

RIEDEL H; SCHLESSINGER J; ULLRICH A

DEP. DEV. BIOL., GENENTECH INC., 460 POINT SAN BRUNO BLVD., SAN  
FRANCISCO, CALIF. 94080, USA.

SCIENCE (WASH D C) 236 (4798). 1987. 197-200. CODEN: SCIEA

Language: ENGLISH

3/3/109 (Item 21 from file: 5)

4885305 BIOSIS Number: 80012616

THE DROSOPHILA EPIDERMAL GROWTH FACTOR RECEPTOR GENE HOMOLOGUE  
CONSERVATION OF BOTH HORMONE BINDING AND KINASE DOMAINS

LIVNEH E; GLAZER L; SEGAL D; SCHLESSINGER J; SHILO B-Z

DEP. CHEM. IMMUNOL., WEIZMANN INSTITUTE OF SCIENCE, REHOVOT 76100,  
ISRAEL.

CELL 40 (3). 1985. 599-608. CODEN: CELLB

Full Journal Title: Cell

Language: ENGLISH

3/3/110 (Item 22 from file: 5)

4458457 BIOSIS Number: 78032280

ANTIGEN INITIATED RELEASE OF PLATELET ACTIVATING FACTOR PAF-ACETHER FROM  
MOUSE BONE MARROW DERIVED MAST CELLS SENSITIZED WITH MONO CLONAL IMMUNO  
GLOBULIN E

MENCIA-HUERTA J-M; LEWIS R A; AUSTEN K F; RAZIN E

DEP. MED., HARVARD MED. SCH., BOSTON, MA 02115.

J IMMUNOL 131 (6). 1983. 2958-2964. CODEN: JOIMA

Full Journal Title: Journal of Immunology

Language: ENGLISH

3/3/111 (Item 1 from file: 399)

119087291 CA: 119(9)87291t JOURNAL

Decreased level of PDGF-stimulated receptor autophosphorylation by  
fibroblasts in mechanically relaxed collagen matrixes

AUTHOR(S): Lin, Ying Chun; Grinnell, Frederick

LOCATION: Southwest. Med. Sch., Univ. Texas, Dallas, TX, 75235, USA

JOURNAL: J. Cell Biol. DATE: 1993 VOLUME: 122 NUMBER: 3 PAGES: 663-72

CODEN: JCLBA3 ISSN: 0021-9525 LANGUAGE: English

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* * * * *
*   The USPTO production files are current through:
*   07 MAR 1995 for U.S. Patent Text Data.
*   07 MAR 1995 for U.S. Current Classification data.
*   07 MAR 1995 for U.S. Patent Image Data.
* * * * *
FILE 'USPAT' ENTERED AT 16:21:40 ON 07 MAR 95

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*           W E L C O M E   T O   T H E
*           U . S .   P A T E N T   T E X T   F I L E
* * * * *

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=> s (human epidermal growth factor receptor 2) or her2 or ngl or
(c(w)erbb?) or erbb?      113386 HUMAN

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      2500 EPIDERMAL
      101383 GROWTH
      193084 FACTOR
      16115 RECEPTOR
      1389356 2

```

```

      0 HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR 2

```

```

(HUMAN(W)EPIDERMAL(W)GROWTH(W)FACTOR(W)RECEPTOR(W)2)

```

```

      3 HER2
      150 NGL
      1023325 C
      41 ERBB?
      10 C(W)ERBB?
      41 ERBB?

```

```

L1      192 (HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR 2) OR HER2
OR NGL O R (
      C(W)ERBB?) OR ERBB?

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=> s 11 and domain?

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```

      21629 DOMAIN?

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L2      26 L1 AND DOMAIN?

```

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=> s 12 and (extracellular or transmembran? or cytoplasm?)

```

```

      3703 EXTRACELLULAR
      1233 TRANSMEMBRAN?
      2948 CYTOPLASM?

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L3      22 L2 AND (EXTRACELLULAR OR TRANSMEMBRAN? OR
CYTOPLASM?)

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```

=> s 13 and soluble.

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      171037 SOLUBLE

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L4      5 L3 AND SOLUBLE

```

```

=> s 13 not 14

```

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L5      17 L3 NOT L4

```

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=> d 14 1-5

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①. 5,367,060, Nov. 22, 1994, Structure, production and use of heregulin; Richard L. Vandlen, et al., 530/399, 350 IMAGE

AVAILABLE]

2. 5,344,760, Sep. 6, 1994, Method of cancer detection; Jeanne P. Harvey, et al., 435/7.5, 7.1, 7.9, 7.92; 436/501, 518, 536 [IMAGE AVAILABLE]

? ~~2~~ 5,256,642, Oct. 26, 1993, Compositions of **\*\*soluble\*\*** complement receptor 1 (CR1) and a thrombolytic agent, and the methods of use thereof; Douglas T. Fearon, et al., 514/8; 424/94.63, 94.64; 435/215, 216; 514/2; 530/350 [IMAGE AVAILABLE]

4. 5,243,041, Sep. 7, 1993, DNA vector with isolated CDNA gene encoding metalloproteinase; Jose A. Fernandez-Pol, 536/23.5, 24.31 [IMAGE AVAILABLE]

5. 5,212,071, May 16, 1993, Nucleic acids encoding a human C3b/C4b receptor (CR1); Douglas T. Fearon, et al., 435/69.1, 252.3, 320.1; 530/350 [IMAGE AVAILABLE]

=> d 14 1,2 ab

US PAT NO: 5,367,060 [IMAGE AVAILABLE]

L4: 1 of 5

ABSTRACT:

A novel polypeptide with binding affinity for the p185.sup.**\*\*HER2\*\*** receptor, designated heregulin-.alpha., has been identified and purified from cultured human cells. DNA sequences encoding additional heregulin polypeptides, designated heregulin-.alpha., heregulin-.beta.1, heregulin-.beta.2, heregulin-.beta.2-like, and heregulin-.beta.3, have been isolated, sequenced and expressed. Provided herein are nucleic acid sequences encoding the amino acid sequences of heregulins useful in the production of heregulins by recombinant means. Further provided are the amino acid sequences of heregulins and purification methods therefor. Heregulins and their antibodies are useful as therapeutic agents and in diagnostic methods.

US PAT NO: 5,344,760 [IMAGE AVAILABLE]

L4: 2 of 5

ABSTRACT:

Diagnostic/prognostic methods are provided for detecting and/or quantitating in the body fluids, preferably serum, of mammals carrying a malignant tumor burden, elevated levels of a portion of the epidermal growth factor receptor (EGFr) which comprises substantially the EGFr ectodomain having a molecular weight in the range of from about 90 kilodaltons (kd) to about 115 kd, preferably from about 95 kd to about 105 kd, and more preferably about 100 kd. Substantially pure compositions comprising said EGFr ectodoman protein and/or fragments thereof are disclosed as well as test kits for performing the disclosed assays.

=> d 15 1-17

1. 5,376,530, Dec. 27, 1994, Steroid/thyroid hormone receptor-related gene, which is inappropriately expressed in human hepatocellular carcinoma, and which is a retinoic acid

receptor; Hughes B. De The, et al., 435/6, 69.1, 172.3; 530/326, 327, 350, 828; 536/23.1, 24.31 [IMAGE AVAILABLE]

2. 5,317,090, May 31, 1994, Steroid/thyroid hormone receptor-related gene, which is inappropriately expressed in human hepatocellular carcinoma, and which is a retinoic acid receptor; Hughes Blandin De The, et al., 530/387.1, 387.9, 388.1, 388.22, 391.1 [IMAGE AVAILABLE]

3. 5,268,477, Feb. 22, 1994, Method for prognosticating response to cancer therapy; Sarah S. Bacus, 424/2, 85.5; 435/7.1; 436/501 [IMAGE AVAILABLE]

4. 5,223,606, Jun. 29, 1993, Steroid/thyroid hormone receptor-related protein inappropriately expressed in human hepatocellular carcinoma; Hughes Blandin de The, et al., 530/350; 435/69.1; 530/828, 846 [IMAGE AVAILABLE]

5. 5,212,290, May 18, 1993, Antibodies specific for type II mutant EGFR; Bert Vogelstein, et al., 530/387.7, 387.1, 388.22, 388.8, 389.1 [IMAGE AVAILABLE]

6. 5,183,884, Feb. 2, 1993, DNA segment encoding a gene for a receptor related to the epidermal growth factor receptor; Matthias H. Kraus, et al., 536/23.5; 435/252.3, 320.1; 536/23.1 [IMAGE AVAILABLE]

7. 5,149,731, Sep. 22, 1992, Steroid/thyroid hormone receptor-related gene inappropriately expressed in human hepatocellular carcinoma; Hugues Blandin de THE, et al., 530/326, 327, 328, 350, 405 [IMAGE AVAILABLE]

8. 5,030,576, Jul. 9, 1991, Receptors for efficient determination of ligands and their antagonists or agonists; Thomas J. Dull, et al., 435/69.7, 69.1; 530/350, 388.22; 536/23.1, 24.1 [IMAGE AVAILABLE]

9. 4,968,603, Nov. 6, 1990, Determination of status in neoplastic disease; Dennis J. Slamon, et al., 435/6, 7.23; 436/94, 501; 935/77, 78 [IMAGE AVAILABLE]

10. 4,957,865, Sep. 18, 1990, Cloning or expression vectors containing the avian erythroblastosis virus genome and cells transfected by these vectors; Jacques Samarut, et al., 435/235.1, 69.1, 317.1, 320.1; 935/32, 57 [IMAGE AVAILABLE]

11. 4,937,232, Jun. 26, 1990, Inhibition of protein kinase C by long-chain bases; Robert M. Bell, et al., 514/26, 28; 536/5 [IMAGE AVAILABLE]

12. 4,935,341, Jun. 19, 1990, Detection of point mutations in neu genes; Cornelia I. Bargmann, et al., 435/6, 803; 436/501; 536/24.3, 24.31; 935/9, 78 [IMAGE AVAILABLE]

13. 4,933,294, Jun. 12, 1990, Method of detecting truncated epidermal growth factor receptors; Michael D. Waterfield, et al., 436/501; 435/4, 7.21, 7.23, 15; 436/503, 518, 813, 815, 817 [IMAGE AVAILABLE]



**\*\*domains\*\*** of the EGF-R and **\*\*erbB\*\***-2 proteins, respectively. cDNA cloning revealed a predicted 140 kd **\*\*transmembrane\*\*** polypeptide with structural features identifying it as a member of the **\*\*erbB\*\*** family, prompting designation of the new gene as **\*\*erbB\*\***-3. It was mapped to human chromosome 12q11-13 and was shown to be expressed as a 6.2 kb transcript in a variety of normal tissues of epithelial origin. Markedly elevated **\*\*erbB\*\***-3 mRNA levels were demonstrated in certain human mammary tumor cell lines. These findings indicate that increased **\*\*erbB\*\***-3 expression, as in the case of EGF-R and **\*\*erbB\*\***-2, plays a role in some human malignancies.

US PAT NO: 4,935,341 [IMAGE AVAILABLE]

L5: 12 of

17

ABSTRACT:

Oligonucleotide probes reactive with regions of neu oncogenes of mammalian origin in which the mutation causing activation of such oncogenes is contained are described, as are methods for their use in detecting the presence of neu oncogenes in tumor cells. Antibodies specific for gene products encoded by neu oncogenes are also described.

US PAT NO: 4,933,294 [IMAGE AVAILABLE]

L5: 13 of

17

ABSTRACT:

Neoplastic and other diseases can be diagnosed by assaying a human test sample e.g. body fluid, tissue or cultured tumor explant cells, for structurally altered or abnormally expressed growth factor receptors or for the RNA transcripts of genes which encode them. For example, the assay can be for truncated EGF receptor having at least a portion of its mature amino terminus deleted. Antibodies, capable of binding a predetermined amino acid sequence within the EGF receptor, are also useful in diagnosis and therapy as are conjugates of an immunogenic polymer bound to a polypeptide fragment of EGF receptor. DNA and RNA encoding EGF receptor or fragments thereof are also described.

=> d his

(FILE 'USPAT' ENTERED AT 16:21:40 ON 07 MAR 95)

L1 192 S (HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR 2) OR  
HER2 OR NG L 0

L2 26 S L1 AND DOMAIN?

L3 22 S L2 AND (EXTRACELLULAR OR TRANSMEMBRAN? OR  
CYTOPLASM?) L4 5 S L3 AND SOLUBLE

L5 17 S L3 NOT L4

=> log y

U.S. Patent & Trademark Office LOGOFF AT 16:29:29 ON 07 MAR 95

2-4-4

OK

ATH

OK

14. 4,859,609, Aug. 22, 1989, Novel receptors for efficient determination of ligands and their antagonists or agonists; Thomas J. Dull, et al., 436/501; 435/7.22, 7.31, 7.9, 968; 436/63, 503, 537; 530/402, 806, 808; 935/81, 109 [IMAGE AVAILABLE]

15. 4,837,237, Jun. 6, 1989, Therapy using glucosidase processing inhibitors; Larry R. Rohrschneider, et al., 514/62; 436/63, 64; 514/23, 283, 345, 729, 738 [IMAGE AVAILABLE]

16. 4,816,450, Mar. 20, 1989, Inhibition of protein kinase C by long-chain bases; Robert M. Bell, et al., 514/25, 23, 26, 28, 54; 536/5 [IMAGE AVAILABLE]

17. 4,774,321, Sep. 27, 1988, DP100 EGF and insulin-binding protein from Drosophila cells; Marsha R. Rosner, et al., 530/350; 436/501; 530/303, 305, 389.1, 389.2, 399, 413 [IMAGE AVAILABLE]

=> d 15 3,6,12,13 ab

US PAT NO: 5,288,477 [IMAGE AVAILABLE]

LS: 3 of

17

ABSTRACT:

A method for prognosticating the effectiveness of a chemotherapy using monoclonal antibodies and ligand molecules. The putative anti-cancer agent has binding specificity for a oncogenic receptor molecule on the membrane of a cancer cell, such as HER-2/neu. When the putative agent binds to the oncogenic receptor, the receptor translocates from the membrane to the **cytoplasm** or perinucleus of the cancer cell, accompanied by a transient increase in the total cellular content of the receptor, and results in terminal cell differentiation. The efficacy of the agent in vivo can be determined in vitro by treatment of biopsied cancer cells with the agent and subsequent examination of the cells for evidence of terminal cell differentiation. Such evidence includes morphological change, reduction in cell growth, or production of chemicals associated with the mature phenotype. Additionally, treated cells may be examined with immunohistochemicals specific for the oncogenic receptor, to determine translocation of the receptor from the membrane to the **cytoplasm** or perinucleus. Quantification of receptor levels in treated cells by measuring optical densities after staining can be used to determine translocation, as well as a transient increase in total cellular content of the receptor.

US PAT NO: 5,183,884 [IMAGE AVAILABLE]

LS: 6 of

17

ABSTRACT:

A DNA fragment distinct from the epidermal growth factor receptor (EGF-R) and **erbB-2** genes was detected by reduced stringency hybridization of v-**erbB** to normal genomic human DNA. Characterization of the cloned DNA fragment mapped the region of v-**erbB** homology to three exons with closest homology of 64% and 67% to a contiguous region within the tyrosine kinase

MONOCLONAL ANTIBODIES DIRECTED AGAINST THE EXTRACELLULAR DOMAIN OF THE  
HER2-ERBB2

KOTTS C E; WIRTH C M; CARVER M E; FENDLY B M  
GENENTECH INC., DEP. MEDICINAL ANALYTICAL CHEMISTRY, S. SAN FRANCISCO,  
CALIF. 94080.

FORTY-FIRST ANNUAL MEETING OF THE TISSUE CULTURE ASSOCIATION, HOUSTON,  
TEXAS, USA, JUNE 10-13, 1990. IN VITRO CELL DEV BIOL 26 (3 PART 2). 1990.  
59A. CODEN: ICDBE

Language: ENGLISH

Document Type: CONFERENCE PAPER

3/3/101 (Item 13 from file: 5)

7044909 BIOSIS Number: 87105430

P185 +HER-2 MONOCLONAL ANTIBODY HAS ANTIPROLIFERATIVE EFFECTS IN-VITRO  
AND SENSITIZES HUMAN BREAST TUMOR CELLS TO TUMOR NECROSIS FACTOR

HUDZIAK R M; LEWIS G D; WINGET M; FENDLY B M; SHEPARD H M; ULLRICH A  
DEP. DEV. BIOL., GENENTECH INC., 460 POINT SAN BRUNO BLVD., SOUTH SAN  
FRANCISCO, CALIF. 94080.

MOL CELL BIOL 9 (3). 1989. 1165-1172. CODEN: MCEBD

Full Journal Title: Molecular and Cellular Biology

Language: ENGLISH

3/3/102 (Item 14 from file: 5)

6974775 BIOSIS Number: 87035296

BIOCHEMICAL AND PHARMACOLOGICAL CHARACTERIZATION OF HUMAN EMBRYO-DERIVED  
PLATELET ACTIVATING FACTOR

COLLIER M; O'NEILL C; AMMIT A J; SAUNDERS D M  
HUMAN REPRODUCTION UNIT, ROYAL NORTH SHORE HOSP., ST. LEONARDS, NSW 2065,  
AUST.

HUM REPROD (OXF) 3 (8). 1988. 993-998. CODEN: HUREE

Full Journal Title: Human Reproduction (Oxford)

Language: ENGLISH

3/3/103 (Item 15 from file: 5)

6640197 BIOSIS Number: 86106748

PHOSPHOLIPASE A-2 INDUCED AIRWAY HYPERREACTIVITY TO COOLING AND  
ACETYLCHOLINE IN RAT TRACHEA PHARMACOLOGICAL MODULATION

CHAND N; DIAMANTIS W; MAHONEY T P; SOFIA R D  
DEP. PHARMACOLOGY, WALLACE LAB., DIV. CARTER-WALLACE INC., CRANBURY, N.J.  
08512.

BR J PHARMACOL 94 (4). 1988. 1057-1062. CODEN: BJPCB

Full Journal Title: British Journal of Pharmacology

Language: ENGLISH

3/3/104 (Item 16 from file: 5)

6633430 BIOSIS Number: 86099981

TRANSIENT INCREASE OF CYTOSOLIC FREE CALCIUM IN CULTURED HUMAN VASCULAR  
ENDOTHELIAL CELLS BY PLATELET-ACTIVATING FACTOR

HIRAFUJI M; MAEYAMA K; WATANABE T; OGURA Y  
DEP. PHARMACOL., TOHOKU UNIV. SCH. DENTISTRY, 4-1 SEIRYO-MACHI, SENDAI  
980, JPN.

BIOCHEM BIOPHYS RES COMMUN 154 (3). 1988. 910-917. CODEN: BBRCA

Full Journal Title: Biochemical and Biophysical Research Communications

Language: ENGLISH

3/3/105 (Item 17 from file: 5)

6617729 BIOSIS Number: 86084280

ROLE OF PAF-ACETHER IN THE MEDIATION OF PATHOPHYSIOLOGICAL RESPONSES TO  
AGGREGATED IMMUNOGLOBULINS STUDIES WITH THE PLATELET-ACTIVATING FACTOR  
RECEPTOR ANTAGONIST BN-52021

FERNANDEZ-GALLARDO S; CANO E; BRAQUET P; SANCHEZ CRESPO M  
INST. INVEST. MED. FUND. JIMENEZ DIAZ, CENT. ASOCIADO CSIC, AV. REYES  
CATOLICOS 2, 28040-MADRID, SPAIN

INT J IMMUNOPHARMACOL 10 (4). 1988. 353-360. CODEN: IJIMD

Full Journal Title: International Journal of Immunopharmacology

Language: ENGLISH

CANCER RESEARCH INST., UNIVERSITY CALIFORNIA, SAN FRANCISCO, CALIF.  
94143-0128.

J BIOL CHEM 266 (22). 1991. 14300-14305. CODEN: JBCHA

Full Journal Title: Journal of Biological Chemistry

Language: ENGLISH

3/3/95 (Item 7 from file: 5)

8211582 BIOSIS Number: 91132582

SELECTION OF MONOCLONAL ANTIBODIES WHICH INDUCE INTERNALIZATION AND  
PHOSPHORYLATION OF P185H-E-R-2 AND GROWTH INHIBITION OF CELLS WITH HER2-NEU  
GENE AMPLIFICATION

TAGLIABUE E; CENTIS F; CAMPIGLIO M; MASTROIANNI A; MARTIGNONE S;

PELLEGRINI R; CASALINI F; LANZI C; MENARD S; COLNAGHI M I

DIV. EXP. ONCOL. E, ISTITUTO NAZIONALE PER LO STUDIO E LA CURA DEI

TUMORI, VIA G. VENEZIAN 1, 20133 MILAN, ITALY.

INT J CANCER 47 (6). 1991. 933-937. CODEN: IJCNA

Full Journal Title: International Journal of Cancer

Language: ENGLISH

3/3/96 (Item 8 from file: 5)

8165749 BIOSIS Number: 91086749

SCINTIGRAPHIC DETECTION OF OVEREXPRESSED C-ERB-B-2 PROTOONCOGENE PRODUCTS  
BY A CLASS-SWITCHED MURINE ANTI-C-ERB-B-2 PROTEIN MONOCLONAL ANTIBODY

SAGA T; ENDO K; AKIYAMA T; SAKAHARA H; KOIZUMI M; WATANABE Y; NAKAI T;

HOSONO M; YAMAMOTO T; ET AL

DEP. NUCL. MED., KYOTO UNIV. HOSP., SHOGGIN, SAKYO-KU, KYOTO 606, JPN.

CANCER RES 51 (3). 1991. 990-994. CODEN: CNREA

Full Journal Title: Cancer Research

Language: ENGLISH

3/3/97 (Item 9 from file: 5)

7761575 BIOSIS Number: 90129575

DISTINCT STIMULATORY EFFECT OF PLATELET-ACTIVATING FACTOR ON

PROSTAGLANDIN I-2 AND THROMBOXANE A-2 BIOSYNTHESIS BY RAT DENTAL PULP

HIRAFUJI M; OGURA Y

DEP. PHARMACOL., TOHOKU UNIV. SCH. DENT., 4-1 SEIRYO-MACHI, SENDAI 980,  
JPN.

EUR J PHARMACOL 185 (1). 1990. 81-90. CODEN: EJPHA

Full Journal Title: European Journal of Pharmacology

Language: ENGLISH

3/3/98 (Item 10 from file: 5)

7743434 BIOSIS Number: 90111434

ELISA FOR QUANTITATION OF THE EXTRACELLULAR DOMAIN OF P185H-E-R-2 IN  
BIOLOGICAL FLUIDS

SIAS P E; KOTTS C E; VETTERLEIN D; SHEPARD M; WONG W L T

IMMUNOL. RES. ASSAY TECHNOLOGIES, GENENTECH INC., 460 POINT SAN BRUNO

BLVD., SOUTH SAN FRANCISCO, CALIF. 94080, USA.

J IMMUNOL METHODS 132 (1). 1990. 73-80. CODEN: JIMMB

Full Journal Title: Journal of Immunological Methods

Language: ENGLISH

3/3/99 (Item 11 from file: 5)

7678519 BIOSIS Number: 90046519

PHARMACOLOGICAL MODULATION OF 2 METHYLCARBAMATE PAF INDUCED RAT PAW EDEMA

CASTRO-FARIA-NETO H C; SILVA P M R; MARTINS M A; SILVA P S; HENRIQUES M G

O M; CORDEIRO R S B; VARGAFTIG B B

DEP. FISILOGIA FARMACODINAMICA, FUNDACAO-OSWALDO CRUZ, AV. BRASIL, 4365

MANGUINHOS, 20010 RIO DE JANEIRO, RJ, BRAZ.

J PHARM PHARMACOL 42 (3). 1990. 203-204. CODEN: JPPMA

Full Journal Title: Journal of Pharmacy and Pharmacology

Language: ENGLISH

3/3/100 (Item 12 from file: 5)

7563000 BIOSIS Number: 39075607

DIFFERENTIAL GROWTH INHIBITION OF HUMAN CARCINOMA CELLS EXPOSED TO

Languages: ENGLISH  
Document type: JOURNAL ARTICLE

3/3/89 (Item 1 from file: 5)  
10453588 BIOSIS Number: 96053588  
ANTIBODY-INDUCED ACTIVATION OF P185H-E-R-2 IN THE HUMAN LUNG  
ADENOCARCINOMA CELL LINE CALU-3 REQUIRES BIVALENCY  
SRINIVAS U; TAGLIAPIETRA E; CAMPIGLIO M; MENARD S; COLNAGHI M I  
DEP. CLIN. CHEM., UNIV. HOSP., LINKÖPING, SWEDEN.  
CANCER IMMUNOL IMMUNOTHER 36 (6). 1993. 397-402. CODEN: CIIMD  
Full Journal Title: Cancer Immunology Immunotherapy  
Language: ENGLISH

3/3/90 (Item 2 from file: 5)  
10278981 BIOSIS Number: 45078981  
A RECOMBINANT SINGLE CHAIN FV FUSION MOLECULE SPECIFICALLY RECOGNIZES THE  
EXTRACELLULAR DOMAIN OF THE ERBB-2 RECEPTOR  
WELLS W; HARWERTH I-M; GRONER B; HYNES N E  
FRIEDRICH MIESCHER INST., P.O. BOX 2543, CH-4002 BASEL, SWITZ.  
MALAVASI, F., R. CORTESE AND A. ALBERTINI (ED.). EUROPEAN BIOTECHNOLOGY  
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ANDOVER, ENGLAND, UK. ISBN 0-946707-48-0. 0 (0). 1992. 159-168. CODEN:  
46344  
Language: ENGLISH  
Document Type: CONFERENCE PAPER

3/3/91 (Item 3 from file: 5)  
9546122 BIOSIS Number: 94051122  
VLA-4-FIBRONECTIN INTERACTION IS REQUIRED FOR THE TERMINAL  
DIFFERENTIATION OF HUMAN BONE MARROW CELLS CAPABLE OF SPONTANEOUS AND HIGH  
RATE IMMUNOGLOBULIN SECRETION  
ROLDAN E; GARCIA-PARDO A; BRIEVA J A  
HOSP. RAMON Y CAJAL, SERVICIO DE INMUNOLOGIA, 28034 MADRID, SPAIN.  
J EXP MED 175 (6). 1992. 1739-1747. CODEN: JEMEA  
Full Journal Title: Journal of Experimental Medicine  
Language: ENGLISH

3/3/92 (Item 4 from file: 5)  
8826738 BIOSIS Number: 42051738  
DETECTION OF TRUNCATED AND ALTERNATIVELY SPLICED TRANSCRIPTS CONTAINING  
HER2-NEU EXTRACELLULAR DOMAIN IN HUMAN BREAST CANCER CELLS  
ROBLES R; SCOTT G K; TRIPATHY D; PARKS J; SHEPARD H M; BENZ C C  
CANCER RESEARCH INST., UNIV. CALIFORNIA, SAN FRANCISCO, CALIF. 94143.  
14TH ANNUAL SAN ANTONIO BREAST CANCER SYMPOSIUM, SAN ANTONIO, TEXAS, USA,  
DECEMBER 6-7, 1991. BREAST CANCER RES TREAT 19 (2). 1991. 204. CODEN:  
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Language: ENGLISH  
Document Type: CONFERENCE PAPER

3/3/93 (Item 5 from file: 5)  
8673109 BIOSIS Number: 92138109  
REQUIREMENTS FOR THE INTERNALIZATION OF A MURINE MONOCLONAL ANTIBODY  
DIRECTED AGAINST THE HER-2-NEU GENE PRODUCT C-ERB-B-2  
MAIER L A; XU F J; HESTER S; BOYER C M; MCKENZIE S; BRUSKIN A M; ARGON Y;  
BAST R C JR  
BOX 3843, DUKE UNIV. MED. CENT., DURHAM, N.C. 27710, USA.  
CANCER RES 51 (19). 1991. 5361-5369. CODEN: CNREA  
Full Journal Title: Cancer Research  
Language: ENGLISH

3/3/94 (Item 6 from file: 5)  
8624596 BIOSIS Number: 9204596  
P185H-E-R-2 SIGNAL TRANSDUCTION IN BREAST CANCER CELLS  
SCOTT G K; DODSON J M; MONTGOMERY P A; JOHNSON R M; SARUP J C; WONG W L;  
UNIVERSITY OF SUEDESBORGEN, U M M, BENZ C C

Languages: ENGLISH  
Document type: JOURNAL ARTICLE

3/3/83 (Item 83 from file: 155)

06651403 88296403

Primary structure of c-kit: relationship with the CSF-1/PDGF receptor kinase family--oncogenic activation of v-kit involves deletion of extracellular domain and C terminus.

Qiu FH; Ray P; Brown K; Barker PE; Jhanwar S; Ruddle FH; Besmer P  
Laboratory of Molecular Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY 10021.

EMBO J Apr 1988, 7 (4) p1003-11, ISSN 0261-4189 Journal Code: EMB

Contract/Grant No.: CA32926; GM09966; CA34775

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/84 (Item 84 from file: 155)

06535975 88180975

Human T-lymphotropic virus type I-associated benign transient immature T-cell lymphocytosis.

Ehrlich GD; Han T; Bettigole R; Merl SA; Lehr B; Tomar RH; Poiesz BJ

Department of Medicine, SUNY HSC, Syracuse 13210.

Am J Hematol Jan 1988, 27 (1) p49-55, ISSN 0361-8609 Journal Code: 3H4

Contract/Grant No.: CA 37478-02

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/85 (Item 85 from file: 155)

06221069 87195069

Transformation by the v-fms oncogene product: an analog of the CSF-1 receptor.

Rettenmier CW; Jackowski S; Rock CO; Roussel MF; Sherr CJ

J Cell Biochem Feb 1987, 33 (2) p109-15, ISSN 0730-2312

Journal Code: HNF

Contract/Grant No.: CA-38187; GM-28035; GM-34496; +

Languages: ENGLISH

Document type: JOURNAL ARTICLE; REVIEW

3/3/86 (Item 86 from file: 155)

06203984 87177984

A chimeric, ligand-binding v-erbB/EGF receptor retains transforming potential.

Riedel H; Schlessinger J; Ullrich A

Science Apr 10 1987, 236 (4798) p197-200, ISSN 0036-8075

Journal Code: UJ7

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/87 (Item 87 from file: 155)

06056270 87030270

Structure and expression of the chicken epidermal growth factor receptor gene locus.

Olofsson B; Pizon V; Zahraoui A; Tavitian A; Therwath A

Eur J Biochem Oct 15 1986, 160 (2) p261-6, ISSN 0014-2956

Journal Code: EMZ

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/88 (Item 88 from file: 155)

05550244 85166244

Epidermal growth factor precursor is related to the translation product of the Moloney sarcoma virus oncogene mos.

Baldwin GS

Proc Natl Acad Sci U S A Apr 1985, 82 (7) p1921-5, ISSN 0027-8424

Journal Code: DU2

3/3/77 (Item 77 from file: 155)  
06959720 89261720  
p185HER2 monoclonal antibody has antiproliferative effects in vitro and sensitizes human breast tumor cells to tumor necrosis factor.  
Hudziak RM; Lewis GD; Winget M; Fendly BM; Shepard HM; Ullrich A  
Department of Developmental Biology, Genentech, Inc., South San Francisco, California 94080.  
Mol Cell Biol Mar 1989, 9 (3) p1165-72, ISSN 0270-7306  
Journal Code: NGY  
Languages: ENGLISH  
Document type: JOURNAL ARTICLE

3/3/78 (Item 78 from file: 155)  
06929615 89231615  
HER2 cytoplasmic domain generates normal mitogenic and transforming signals in a chimeric receptor.  
Lee J; Dull TJ; Lax I; Schlessinger J; Ullrich A  
Department of Developmental Biology, Genentech, Inc., South San Francisco, CA 94080.  
EMBO J Jan 1989, 8 (1) p167-73, ISSN 0261-4189 Journal Code: EMB  
Languages: ENGLISH  
Document type: JOURNAL ARTICLE

3/3/79 (Item 79 from file: 155)  
06929614 89231614  
A chimeric EGF-R-neu proto-oncogene allows EGF to regulate neu tyrosine kinase and cell transformation.  
Lehvaslaiho H; Lehtola L; Sistonen L; Alitalo K  
Department of Virology and Pathology, University of Helsinki, Finland.  
EMBO J Jan 1989, 8 (1) p159-66, ISSN 0261-4189 Journal Code: EMB  
Languages: ENGLISH  
Document type: JOURNAL ARTICLE

3/3/80 (Item 80 from file: 155)  
06911528 89213528  
A murine monoclonal antibody that recognizes an extracellular domain of the human c-erbB-2 protooncogene product.  
Masuko T; Sugahara K; Kozono M; Otsuki S; Akiyama T; Yamamoto T; Toyoshima K; Hashimoto Y  
Department of Hygienic Chemistry, Tohoku University, Sendai.  
Jpn J Cancer Res Jan 1989, 80 (1) p10-4, ISSN 0910-5050  
Journal Code: HBA  
Languages: ENGLISH  
Document type: JOURNAL ARTICLE

3/3/81 (Item 81 from file: 155)  
06899873 89201873  
Analysis of mammalian fibroblast transformation by normal and mutated human EGF receptors.  
Haley JD; Hsuan JJ; Waterfield MD  
Ludwig Institute for Cancer Research, London, UK.  
Oncogene Mar 1989, 4 (3) p273-83, ISSN 0950-9232 Journal Code: ONC  
Languages: ENGLISH  
Document type: JOURNAL ARTICLE

3/3/82 (Item 82 from file: 155)  
06740123 89042123  
neu protooncogene fused to an immunoglobulin heavy chain gene requires immunoglobulin light chain for cell surface expression and oncogenic transformation.  
Flanagan JG; Leder P  
Howard Hughes Medical Institute, Harvard Medical School, Boston, MA 02115.  
Proc Natl Acad Sci U S A Nov 1988, 85 (21) p8057-61, ISSN 0027-8424

Oncogene Jun 1990, 5 (6) p815-21, ISSN 0950-9232 Journal Code: ONC  
Languages: ENGLISH  
Document type: JOURNAL ARTICLE

3/3/72 (Item 72 from file: 155)

07369434 90276434

Enhancement of tyrosine kinase activity of the Drosophila epidermal growth factor receptor homolog by alterations of the transmembrane domain.

Wides RJ; Zak NB; Shilo BZ

Department of Molecular Genetics and Virology, Weizmann Institute of Science, Rehovot, Israel.

Eur J Biochem May 20 1990, 189 (3) p637-45, ISSN 0014-2956

Journal Code: EMZ

Contract/Grant No.: GM35998, GM, NIGMS; CA08501, CA, NCI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/73 (Item 73 from file: 155)

07351896 90258896

Epidermal growth factor receptor cytoplasmic domain mutations trigger ligand-independent transformation.

Massaglia S; Gray A; Dull TJ; Munemitsu S; Kun HJ; Schlessinger J; Ullrich A

Department of Developmental Biology, Genentech, Inc., South San Francisco, California 94080.

Mol Cell Biol Jun 1990, 10 (6) p3048-55, ISSN 0270-7306

Journal Code: NGY

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/74 (Item 74 from file: 155)

07296065 90203065

Regulation by EGF is maintained in an overexpressed chimeric EGFR/neu receptor tyrosine kinase.

Lehvaslaiho H; Sistonen L; diRenzo F; Partanen J; Comoglio P; Holtta E; Alitalo K

Department of Virology, University of Helsinki, Finland.

J Cell Biochem Mar 1990, 42 (3) p123-33, ISSN 0730-2312

Journal Code: HNF

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/75 (Item 75 from file: 155)

07243117 90150117

Characterization of murine monoclonal antibodies reactive to either the human epidermal growth factor receptor or HER2/neu gene product.

Fendly BM; Winget M; Hudziak RM; Lipari MT; Napier MA; Ullrich A

Department of Medicinal and Analytical Chemistry, Genentech, Inc., South San Francisco, California 94080.

Cancer Res Mar 1 1990, 50 (5) p1550-8, ISSN 0008-5472

Journal Code: CNF

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/76 (Item 76 from file: 155)

07151585 90058585

Analysis of c-erbB-2 expression in breast carcinomas with clinical follow-up.

Thor AD; Schwartz LH; Koerner FC; Edgerton SM; Skates SJ; Yin S; McKenzie SJ; Panicali DL; Marks PJ; Fingert HJ; et al

Department of Pathology, Massachusetts General Hospital, Boston 02114.

Cancer Res Dec 15 1989, 49 (24 Pt 1) p7147-52, ISSN 0008-5472

Journal Code: CNF

Contract/Grant No.: P01 CA44768

Languages: ENGLISH

Document type: JOURNAL ARTICLE



3/3/66 (Item 66 from file: 155)

07554143 91073143

The extracellular domain of HER2/neu is a potential immunogen for active specific immunotherapy of breast cancer.

Fendly BM; Kotts C; Vetterlein D; Lewis GD; Winget M; Carver ME; Watson SR; Sarup J; Saks S; Ullrich A; et al

Genentech, Inc., South San Francisco, CA 94080.

J Biol Response Mod Oct 1990, 9 (5) p449-55, ISSN 0732-6580

Journal Code: JBM

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/67 (Item 67 from file: 155)

07468374 90375374

Induction of growth factor-receptor and metalloproteinase genes by epidermal growth factor and/or transforming growth factor-alpha in human gastric carcinoma cell line MKN-28.

Yoshida K; Tsujino T; Yasui W; Kameda T; Sano T; Nakayama H; Toge T; Tahara E

First Department of Pathology, Hiroshima University School of Medicine.

Jpn J Cancer Res Aug 1990, 81 (8) p793-8, ISSN 0910-5050

Journal Code: HBA

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/68 (Item 68 from file: 155)

07454943 90361943

ELISA for quantitation of the extracellular domain of p185HER2 in biological fluids.

Sias PE; Kotts CE; Vetterlein D; Shepard M; Wong WL

Department of Immunology Research and Assay Technologies, Genentech Inc., So. San Francisco, CA 94080.

J Immunol Methods Aug 28 1990, 132 (1) p73-80, ISSN 0022-1759

Journal Code: IFE

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/69 (Item 69 from file: 155)

07452495 90359495

Molecular, biochemical, and cellular biology of human breast cancer.

Smith HS

Geraldine Brush Cancer Research Institute, Pacific-Presbyterian Medical Center, San Francisco, California 94115.

Cancer Cells Apr 1990, 2 (4) p123-5, ISSN 1042-2196 Journal Code:

AUS

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/70 (Item 70 from file: 155)

07440036 90347036

Soluble Fc gamma receptor III in human plasma originates from release by neutrophils.

Huizinga TW; de Haas M; Kleijer M; Nuijens JH; Roos D; von dem Borne AE

Central Laboratory of The Netherlands Red Cross Blood Transfusion Service, Amsterdam.

J Clin Invest Aug 1990, 86 (2) p416-23, ISSN 0021-9738

Journal Code: HS7

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/71 (Item 71 from file: 155)

07388274 90295274

Downregulation of the epidermal growth factor response in neu oncogene-transformed cells.

Sistonen L; Koskinen PJ; Lehtola L; Bravo R; Alitalo K

Department of Urology, University of Helsinki, Finland.

Pellegrini R; Casalini P; Lanzi C; Menard S; Colnaghi MI  
Division of Experimental Oncology E, Istituto Nazionale per lo Studio e  
la Cura dei Tumori, Milan, Italy  
Int J Cancer Apr 1 1991, 47 (6) p933-7, ISSN 0020-7136  
Journal Code: GQU  
Languages: ENGLISH  
Document type: JOURNAL ARTICLE

3/3/61 (Item 61 from file: 155)  
07651140 91170140  
Isolation and characterization of new mammalian kinase genes by cross  
hybridization with a tyrosine kinase probe.  
Shibuya M; Matsushime H; Yamane A; Ikeda T; Yoshida MC; Tojo A  
Department of Genetics, University of Tokyo, Japan.  
Int Symp Princess Takamatsu Cancer Res Fund 1989, 20 p103-10,  
Journal Code: HHI  
Languages: ENGLISH  
Document type: JOURNAL ARTICLE

3/3/62 (Item 62 from file: 155)  
07626180 91145180  
The presence of c-erbB-2 gene product-related protein in culture medium  
conditioned by breast cancer cell line SK-BR-3.  
Alper O; Yamaguchi K; Hitomi J; Honda S; Matsushima T; Abe K  
Growth Factor Division, National Cancer Center Research Institute, Tokyo,  
Japan.  
Cell Growth Differ Dec 1990, 1 (12) p591-9, ISSN 1044-9523  
Journal Code: AYH  
Languages: ENGLISH  
Document type: JOURNAL ARTICLE

3/3/63 (Item 63 from file: 155)  
07589899 91108899  
Expression of c-erbB-2 gene product in urinary bladder cancer.  
Moriyama M; Akiyama T; Yamamoto T; Kawamoto T; Kato T; Sato K; Watanuki T  
; Hikage T; Katsuta N; Mori S  
Department of Pathology and Oncology, Institute of Medical Science,  
University of Tokyo, Japan.  
J Urol Feb 1991, 145 (2) p423-7, ISSN 0022-5347 Journal Code: KC7  
Languages: ENGLISH  
Document type: JOURNAL ARTICLE

3/3/64 (Item 64 from file: 155)  
07588672 91107672  
The extracellular domain of p185/neu is released from the surface of  
human breast carcinoma cells, SK-BR-3.  
Zabrecky JR; Lam T; McKenzie SJ; Carney W  
Applied bioTechnology, Inc., Cambridge, Massachusetts 02142.  
J Biol Chem Jan 25 1991, 266 (3) p1716-20, ISSN 0021-9258  
Journal Code: HIV  
Languages: ENGLISH  
Document type: JOURNAL ARTICLE

3/3/65 (Item 65 from file: 155)  
07586737 91105737  
Scintigraphic detection of overexpressed c-erbB-2 protooncogene products  
by a class-switched murine anti-c-erbB-2 protein monoclonal antibody.  
Saga T; Endo K; Akiyama T; Sakahara H; Koizumi M; Watanabe Y; Nakai T;  
Hosono M; Yamamoto T; Toyoshima K; et al  
Department of Nuclear Medicine, Kyoto University School of Medicine,  
Japan.  
Cancer Res Feb 1 1991, 51 (3) p990-4, ISSN 0008-5472 Journal Code:  
CNF  
Languages: ENGLISH  
Document type: JOURNAL ARTICLE

3/3/55 (Item 55 from file: 155)

07789257 91308257

Modulation of EGF receptor protooncogene expression by growth factors and hormones in human breast carcinoma cells.

Fernandez-Pol JA

Laboratory of Molecular Oncology, Veterans Administration Medical Center, St. Louis, MO 63106.

Crit Rev Oncog 1991, 2 (2) p173-85, ISSN 0893-9675 Journal Code: A1Y

Languages: ENGLISH

Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL

3/3/56 (Item 56 from file: 155)

07774080 91293080

Oncogenic forms of the neu/HER2 tyrosine kinase are permanently coupled to phospholipase C gamma.

Peles E; Levy RB; Or E; Ullrich A; Yarden Y

Department of Chemical Immunology, Weizmann Institute of Science, Rehovot, Israel.

EMBO J Aug 1991, 10 (8) p2077-86, ISSN 0261-4189 Journal Code: EMB

Contract/Grant No.: R01 CA51712, CA, NCI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/57 (Item 57 from file: 155)

07696596 91215596

An antigen immunologically related to the external domain of gp185 is shed from nude mouse tumors overexpressing the c-erbB-2 (HER-2/neu) oncogene.

Langton BC; Crenshaw MC; Chao LA; Stuart SG; Akita RW; Jackson JE

Department of Immunology, Berlex Biosciences Inc., Alameda, California 94501.

Cancer Res May 15 1991, 51 (10) p2593-8, ISSN 0008-5472

Journal Code: CNF

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/58 (Item 58 from file: 155)

07688985 91207985

Cytotoxic T lymphocyte recognition of the H-2-erbB hybrid gene product lacking the complete H-2 domain structure.

Ding L; Isobe K; Iwamoto T; Yoshida T; Nagase F; Kawashima K; Nakashima I

Department of Immunology, Nagoya University School of Medicine, Japan.

Int Immunol 1990, 2 (1) p91-7, ISSN 0953-8178 Journal Code: AY5

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/59 (Item 59 from file: 155)

07688091 91207091

[Laron type dwarfism. Study of GH binding protein in 3 cases]

Le nanisme de type Laron. Etude de la proteine liante de la GH dans 3 observations.

Aguirre A; Donnadiou M; Job JC; Chaussain JL

Service d'Endocrinologie Pediatrique, Hopital Saint-Vincent-de-Paul, Paris.

Arch Fr Pediatr Jan 1991, 48 (1) p5-9, ISSN 0003-9764

Journal Code: 71Q

Languages: FRENCH Summary Languages: ENGLISH

Document type: JOURNAL ARTICLE English Abstract

3/3/60 (Item 60 from file: 155)

07665915 91184915

Selection of monoclonal antibodies which induce internalization and phosphorylation of p185HER2 and growth inhibition of cells with HER2/NEU gene amplification.

3/3/50 (Item 50 from file: 155)

07846853 91365853

Monoclonal antibody therapy of human cancer: taking the HER2 protooncogene to the clinic.

Shepard HM; Lewis GD; Sarup JC; Fendly BM; Maneval D; Mordenti J; Figari I; Kotts CE; Palladino MA Jr; Ullrich A; et al

Department of Developmental Biology, Genentech, Inc., South San Francisco, California 94080.

J Clin Immunol May 1991, 11 (3) p117-27, ISSN 0271-9142

Journal Code: HRC

Languages: ENGLISH

Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL

3/3/51 (Item 51 from file: 155)

07823680 91342680

The amino-terminal 14 amino acids of v-src can functionally replace the extracellular and transmembrane domains of v-erbB.

McMahon M; Schatzman RC; Bishop JM

Department of Microbiology and Immunology, University of California, San Francisco 94143.

Mol Cell Biol Sep 1991, 11 (9) p4760-70, ISSN 0270-7306

Journal Code: NGY

Contract/Grant No.: CA 44338, CA, NCI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/52 (Item 52 from file: 155)

07818091 91337091

Deletion-mutant epidermal growth factor receptor in human gliomas: effects of type II mutation on receptor function.

Humphrey PA; Gangarosa LM; Wong AJ; Archer GE; Lund-Johansen M; Bjerkvig R; Laerum OD; Friedman HS; Bigner DD

Departments of Pathology, Duke University Medical Center, Durham, NC 27710.

Biochem Biophys Res Commun Aug 15 1991, 178 (3) p1413-20, ISSN 0006-291X Journal Code: 9Y8

Contract/Grant No.: NS20023-05, NS, NINDS; T32N507304; CA11898, CA, NCI;

+

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/53 (Item 53 from file: 155)

07810303 91329303

The normal erbB-2 product is an atypical receptor-like tyrosine kinase with constitutive activity in the absence of ligand.

Lonardo F; Di Marco E; King CR; Pierce JH; Segatto O; Aaronson SA; Di Fiore PP

Laboratory of Molecular and Cellular Biology, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892.

New Biol Nov 1990, 2 (11) p992-1003, ISSN 1043-4674 Journal Code: AZH

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/54 (Item 54 from file: 155)

07798780 91317780

p185HER2 signal transduction in breast cancer cells.

Scott GK; Dodson JM; Montgomery PA; Johnson RM; Sarup JC; Wong WL; Ullrich A; Shepard HM; Benz CC

Cancer Research Institute, University of California, San Francisco 94143.

J Biol Chem Aug 5 1991, 266 (22) p14300-5, ISSN 0021-9258

Journal Code: HIV

Contract/Grant No.: CA-44768, CA, NCI; CA-36773, CA, NCI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Int J Cancer Jan 2 1992, 50 (1) p64-8, ISSN 0020-7136  
Journal Code: GQU  
Languages: ENGLISH  
Document type: JOURNAL ARTICLE

3/3/45 (Item 45 from file: 155)

07901091 92039091

Isolation of a cDNA encoding a potential soluble receptor for human erythropoietin.

Todokoro K; Kuramochi S; Nagasawa T; Abe T; Ikawa Y

Tsukuba Life Science Center, Institute of Physical and Chemical Research (RIKEN), Ibaraki, Japan.

Gene Oct 15 1991, 106 (2) p283-4, ISSN 0378-1119 Journal Code: FOP

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/46 (Item 46 from file: 155)

07892123 92030123

Cytometrically coherent transfer of receptor proteins on microporous membranes.

McGrath CM; Grudzien JL; Decker DA; Robbins TO

Grace Bio-Oncology Laboratory, Inc., Pontiac, MI 48342.

Biotechniques Sep 1991, 11 (3) p352-4, 356, 358-61, ISSN 0736-6205

Journal Code: AN3

Contract/Grant No.: CA 51595, CA, NCI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/47 (Item 47 from file: 155)

07882917 92020917

Mechanistic aspects of the opposing effects of monoclonal antibodies to the ERBB2 receptor on tumor growth.

Stancovski I; Hurwitz E; Leitner O; Ullrich A; Yarden Y; Sela M

Department of Chemical Immunology, Weizmann Institute of Science, Rehovot, Israel.

Proc Natl Acad Sci U S A Oct 1 1991, 88 (19) p8691-5, ISSN 0027-8424

Journal Code: PV3

Contract/Grant No.: CA 51712, CA, NCI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/48 (Item 48 from file: 155)

07882897 92020897

Characterization of a neu/c-erbB-2 protein-specific activating factor.

Dobashi K; Davis JG; Mikami Y; Freeman JK; Hamuro J; Greene MI

Division of Immunology, University of Pennsylvania School of Medicine, Philadelphia.

Proc Natl Acad Sci U S A Oct 1 1991, 88 (19) p8582-6, ISSN 0027-8424

Journal Code: PV3

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/49 (Item 49 from file: 155)

07867459 92005459

Requirements for the internalization of a murine monoclonal antibody directed against the HER-2/neu gene product c-erbB-2.

Maier LA; Xu FJ; Hester S; Boyer CM; McKenzie S; Bruskin AM; Argon Y; Bast RC Jr

Department of Medicine, Duke Comprehensive Cancer Center, Duke University Medical Center, Durham, North Carolina 27710.

Cancer Res Oct 1 1991, 51 (19) p5361-9, ISSN 0008-5472

Journal Code: CNF

Contract/Grant No.: 5-R01-CA 51930, CA, NCI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Franklin CC; Kraft AS  
Department of Medicine, University of Alabama, Birmingham 35294  
Biochim Biophys Acta Mar 10 1992, 1134 (2) p137-42, ISSN 0167-3002  
Journal Code: A0W  
Contract/Grant No.: R01 CA42533-04, CA, NCI; CA09128, CA, NCI  
Languages: ENGLISH  
Document type: JOURNAL ARTICLE

3/3/40 (Item 40 from file: 155)

08058103 92196103

Characterization of a growth factor that binds exclusively to the erbB-2 receptor and induces cellular responses.

Lupu R; Colomer R; Kannan B; Lippman ME

Vincent T. Lombardi Cancer Research Center, Georgetown University Medical Center, Washington, DC 20007.

Proc Natl Acad Sci U S A Mar 15 1992, 89 (6) p2287-91, ISSN 0027-8424

Journal Code: PV3

Contract/Grant No.: CA55406-01, CA, NCI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/41 (Item 41 from file: 155)

07990470 92128470

The role of non-ras transforming genes in chemical carcinogenesis.

Cooper CS

Section of Molecular Carcinogenesis, Institute of Cancer Research, Sutton, Surrey, UK.

Environ Health Perspect Jun 1991, 93 p33-40, ISSN 0091-6765

Journal Code: E10

Languages: ENGLISH

Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL

3/3/42 (Item 42 from file: 155)

07985214 92123214

An alternatively processed mRNA from the avian c-erbB gene encodes a soluble, truncated form of the receptor that can block ligand-dependent transformation.

Flickinger TW; Maihle NJ; Kung HJ

Department of Molecular Biology and Microbiology, Case Western Reserve University School of Medicine, Cleveland, Ohio 44106.

Mol Cell Biol Feb 1992, 12 (2) p883-93, ISSN 0270-7306

Journal Code: NGY

Contract/Grant No.: HD 07104-11, HD, NICHD; CA 39207, CA, NCI; CA 51197, CA, NCI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/43 (Item 43 from file: 155)

07985175 92123175

Anti-oncogenic activity of signalling-defective epidermal growth factor receptor mutants.

Redemann N; Holzmann B; von Ruden T; Wagner EF; Schlessinger J; Ullrich A

Department of Molecular Biology, Max-Planck-Institut für Biochemie, Martinsried, Germany.

Mol Cell Biol Feb 1992, 12 (2) p491-8, ISSN 0270-7306

Journal Code: NGY

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/44 (Item 44 from file: 155)

07960213 92098213

Effects of interferons on the expression of the proto-oncogene HER-2 in human ovarian carcinoma cells.

Marth C; Cronauer MV; Doppler W; Ofner D; Ullrich A; Daxenbichler G

Department of Obstetrics and Gynecology, Innsbruck University Clinic,

Document type: JOURNAL ARTICLE

3/3/34 (Item 34 from file: 155)  
08184244 92322244

A chimeric EGFR/neu receptor in functional analysis of the neu oncoprotein.

Lehtola L; Lehvaslaiho H; Koskinen P; Alitalo K

Department of Virology, University of Helsinki, Finland.

Acta Oncol 1992, 31 (2) p147-50, ISSN 0284-186X Journal Code: AON

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/35 (Item 35 from file: 155)  
08181543 92319543

erbB-2 autophosphorylation is required for mitogenic action and high-affinity substrate coupling.

Segatto O; Lonardo F; Helin K; Wexler D; Fazioli F; Rhee SG; Di Fiore PP

Laboratory of Cellular and Molecular Biology, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892.

Oncogene Jul 1992, 7 (7) p1339-46, ISSN 0950-9232 Journal Code: ONC

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/36 (Item 36 from file: 155)  
08161083 92299083

The effects of the normal and oncogenic forms of the neu tyrosine kinase, and the corresponding forms of an immunoglobulin E receptor/neu tyrosine kinase fusion protein, on *Xenopus* oocyte maturation.

Narasimhan V; Hamill O; Cerione RA

Department of Pharmacology, Cornell University, Ithaca, NY 14853-6401.

FEBS Lett Jun 1 1992, 303 (2-3) p164-8, ISSN 0014-5793

Journal Code: EUH

Contract/Grant No.: GM40654, GM, NIGMS

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/37 (Item 37 from file: 155)  
08119596 92257596

Neu differentiation factor: a transmembrane glycoprotein containing an EGF domain and an immunoglobulin homology unit.

Wen D; Peles E; Cupples R; Suggs SV; Bacus SS; Luo Y; Trail G; Hu S; Silbiger SM; Levy RB; et al

Department of Chemical Immunology, Weizmann Institute of Science, Rehovot, Israel.

Cell May 1 1992, 69 (3) p559-72, ISSN 0092-8674 Journal Code: CQ4

Contract/Grant No.: CA-51712, CA, NCI; CA-50843, CA, NCI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/38 (Item 38 from file: 155)  
08096998 92234998

Increased oncogenic potential of ErbB is associated with the loss of a COOH-terminal domain serine phosphorylation site.

Theroux SJ; Taglienti-Sian C; Nair N; Countaway JL; Robinson HL; Davis RJ

Howard Hughes Medical Institute, University of Massachusetts Medical School, Worcester 01605.

J Biol Chem Apr 25 1992, 267 (12) p7967-70, ISSN 0021-9258

Journal Code: HIV

Contract/Grant No.: CA39240, CA, NCI; CA27223, CA, NCI; CA53396, CA, NCI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/39 (Item 39 from file: 155)  
08070001 92208001

Protein kinase C-independent activation of c-jun and c-fos transcription

Alternative splicing of the Schistosoma mansoni gene encoding a homologue of epidermal growth factor receptor.

Shoemaker CB; Ramachandran H; Landa A; dos Reis MG; Stein LD  
Department of Tropical Public Health, Harvard School of Public Health, Boston, MA 02115.

Mol Biochem Parasitol Jul 1992, 53 (1-2) p17-32, ISSN 0166-6851

Journal Code: NOR

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/29 (Item 29 from file: 155)

08226467 92364467

[Role of p185c-erbB2 in endometrial cancer growth in vitro]

Sakamoto H; Ohtani K; Ohta H; Takami M; Takami T; Satoh K

Department of Obstetrics and Gynecology, Nihon University, Faculty of Medicine, Tokyo.

Nippon Sanka Fujinka Gakkai Zasshi Jul 1992, 44 (7) p800-4, ISSN 0300-9165 Journal Code: INR

Languages: JAPANESE Summary Languages: ENGLISH

Document type: JOURNAL ARTICLE English Abstract

3/3/30 (Item 30 from file: 155)

08225416 92363416

p185 HER2/neu epitope mapping with murine monoclonal antibodies.

Centis F; Tagliabue E; Uppugunduri S; Pellegrini R; Martignone S; Mastroianni A; Menard S; Colnaghi M

Division of Experimental Oncology E, Istituto Nazionale per lo Studio e la Cura dei Tumori, Milan, Italy.

Hybridoma Jun 1992, 11 (3) p267-76, ISSN 0272-457X Journal Code: GFS

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/31 (Item 31 from file: 155)

08202569 92340569

Monoclonal antibodies against the extracellular domain of the erbB-2 receptor function as partial ligand agonists.

Harwerth IM; Wels W; Marte BM; Hynes NE

Friedrich Miescher Institute, Basel, Switzerland.

J Biol Chem Jul 25 1992, 267 (21) p15160-7, ISSN 0021-9258  
Journal Code: HIV

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/32 (Item 32 from file: 155)

08200095 92338095

Extracellular calcium mimics the actions of platelet-derived growth factor on mouse fibroblasts.

Epstein RJ; Druker BJ; Irminger JC; Jones SD; Roberts TM; Stiles CD

Department of Medicine, Harvard Medical School, Boston, Massachusetts.

Cell Growth Differ Mar 1992, 3 (3) p157-64, ISSN 1044-9523  
Journal Code: AYH

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/33 (Item 33 from file: 155)

08194477 92332477

Biochemical comparisons of the normal and oncogenic forms of insect cell-expressed neu tyrosine kinases.

Guy PM; Carraway KL III; Cerione RA

Department of Biochemistry, Molecular, and Cell Biology, Cornell University, Ithaca, New York 14853-6401.

J Biol Chem Jul 15 1992, 267 (20) p13851-6, ISSN 0021-9258  
Journal Code: HIV

Contract/Grant No.: GM40654, GM, NIGMS

Languages: ENGLISH



Basel, Switzerland.

Cancer Res (UNITED STATES) Nov 15 1992, 52 (22) p6310-7, ISSN

0008-5472 Journal Code: CNF

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/23 (Item 23 from file: 155)

08303814 93013814

Production and characterization of murine mAbs to the extracellular domain of human neu oncogene product GP185HER2.

Digiesi G; Giacomini P; Fraioli R; Mariani M; Nicotra MR; Segatto O; Natali PG

Laboratory of Immunology, Regina Elena Cancer Institute, Rome, Italy.

Hybridoma Aug 1992, 11 (4) p519-27, ISSN 0272-457X Journal Code:

GFS

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/24 (Item 24 from file: 155)

08301020 93011020

The Xmrk receptor tyrosine kinase is activated in Xiphophorus malignant melanoma.

Wittbrodt J; Lammers R; Malitschek B; Ullrich A; Schartl M

Max-Planck Institute for Biochemistry, Martinsried, Germany.

EMBO J Nov 1992, 11 (11) p4239-46, ISSN 0261-4189 Journal Code: EMB

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/25 (Item 25 from file: 155)

08261282 92399282

Diminution of antibodies directed against tumor cell surface epitopes: a single chain Fv fusion molecule specifically recognizes the extracellular domain of the c-erbB-2 receptor.

Wels W; Harwerth IM; Hynes NE; Groner B

Friedrich Miescher Institute, Basel, Switzerland.

J Steroid Biochem Mol Biol Sep 1992, 43 (1-3) p1-7, ISSN 0960-0760  
Journal Code: AX4

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/26 (Item 26 from file: 155)

08250963 92388963

Elevated soluble c-erbB-2 antigen levels in the serum and effusions of a proportion of breast cancer patients.

Leitzel K; Teramoto Y; Sampson E; Mauceri J; Langton BC; Demers L; Podczaski E; Harvey H; Shambaugh S; Volas G; et al

Department of Medicine, Pennsylvania State University College of Medicine, Milton S. Hershey Medical Center, Hershey, PA 17033.

J Clin Oncol Sep 1992, 10 (9) p1436-43, ISSN 0732-183X  
Journal Code: JCO

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/27 (Item 27 from file: 155)

08228172 92366172

Transformation mediated by the human HER-2 gene independent of the epidermal growth factor receptor.

Chazin VR; Kaleko M; Miller AD; Slamon DJ

Department of Medicine, University of California, Los Angeles.

Oncogene Sep 1992, 7 (9) p1859-66, ISSN 0950-9232 Journal Code: ONC

Contract/Grant No.: CA 36827, CA, NCI; GM-07185, GM, NIGMS

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/28 (Item 28 from file: 155)

08227707 92365707

Massachusetts Medical School, Worcester 01655.

J Virol (UNITED STATES) Feb 1993, 67 (2) p1132-6, ISSN 0022-538X

Journal Code: KCV

Contract/Grant No.: CA27223, CA, NCI; CA23086, CA, NCI; CA58396, CA, NCI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/18 (Item 18 from file: 155)

08403351 93113351

Overproduction of full-length and truncated human estrogen receptors in Escherichia coli.

Ahrens H; Schuh TJ; Rainish BL; Furlow JD; Gorski J; Mueller GC

McArdle Laboratory for Cancer Research, University of Wisconsin-Madison 53706.

Receptor (UNITED STATES) Summer 1992, 2 (2) p77-92, ISSN 1052-8040

Journal Code: BNX

Contract/Grant No.: CA23076, CA, NCI; CA07175, CA, NCI; HD08192, HD, NICHD

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/19 (Item 19 from file: 155)

08395424 93105424

A human tumor xenograft model of therapy with a bispecific monoclonal antibody targeting c-erbB-2 and CD16.

Weiner LM; Holmes M; Adams GP; LaCreta F; Watts P; Garcia de Palazzo I

Department of Medical Oncology, Fox Chase Cancer Center, Philadelphia, Pennsylvania 19111.

Cancer Res (UNITED STATES) Jan 1 1993, 53 (1) p94-100, ISSN 0008-5472

Journal Code: CNF

Contract/Grant No.: CA50633, CA, NCI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/20 (Item 20 from file: 155)

08386493 93096493

Overexpression of the c-MET/HGF receptor gene in human thyroid carcinomas.

Di Renzo MF; Olivero M; Ferro S; Prat M; Bongarzone I; Pilotti S; Belfiore A; Costantino A; Vigneri R; Pierotti MA; et al

Department of Biomedical Science and Oncology, University of Torino Medical School, Italy.

Oncogene (ENGLAND) Dec 1992, 7 (12) p2549-53, ISSN 0950-9232

Journal Code: ONC

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/21 (Item 21 from file: 155)

08381810 93091810

Characterization of an anti-p185HER2 monoclonal antibody that stimulates receptor function and inhibits tumor cell growth.

Sarup JC; Johnson RM; King KL; Fendly BM; Lipari MT; Napier MA; Ullrich A; Shepard HM

Department of Developmental Biology, Genentech, Inc., South San Francisco, California 94080.

Growth Regul (SCOTLAND) Jun 1991, 1 (2) p72-82, ISSN 0956-523X

Journal Code: BNP

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/22 (Item 22 from file: 155)

08336136 93046136

Selective inhibition of tumor cell growth by a recombinant single-chain antibody-toxin specific for the erbB-2 receptor.

Wels W; Harwerth IM; Mueller M; Groner B; Hynes NE

European Molecular Biology Laboratory, Outstation, Heidelberg, 69006

Amplification and overexpression of the erbB-2 gene in human tumors: its involvement in tumor development, significance as a prognostic factor, and potential as a target for cancer therapy.

Hynes NE

Friedrich Miescher Institute, Basel, Switzerland.

Semin Cancer Biol (UNITED STATES) Feb 1993, 4 (1) p19-26, ISSN 1044-579X Journal Code: A6Y

Languages: ENGLISH

Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL

3/3/13 (Item 13 from file: 155)

08479574 93189574

Ligand-specific activation of HER4/p180erbB4, a fourth member of the epidermal growth factor receptor family.

Plowman GD; Culouscou JM; Whitney GS; Green JM; Carlton GW; Foy L; Neubauer MG; Shoyab M

Bristol-Myers Squibb Pharmaceutical Research Institute, Seattle, WA 98121.

Proc Natl Acad Sci U S A (UNITED STATES) Mar 1 1993, 90 (5) p1746-50, ISSN 0027-8424 Journal Code: PV3

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/14 (Item 14 from file: 155)

08451295 93161295

Cell growth regulation in epithelial ovarian cancer.

Bast RC Jr; Boyer CM; Jacobs I; Xu FJ; Wu S; Wiener J; Kohler M; Berchuck A

Department of Medicine, Duke University Medical Center, Durham, North Carolina 27710.

Cancer (UNITED STATES) Feb 15 1993, 71 (4 Suppl) p1597-601, ISSN 0008-543X Journal Code: CLZ

Contract/Grant No.: R01CA39930, CA, NCI

Languages: ENGLISH

Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL

3/3/15 (Item 15 from file: 155)

08449993 93159993

The human EGF receptor as a target for cancer therapy: six new rat mAbs against the receptor on the breast carcinoma MDA-MB 468.

Modjtahedi H; Styles JM; Dean CJ

Section of Immunology, Institute of Cancer Research, Sutton, Surrey, UK.

Br J Cancer (ENGLAND) Feb 1993, 67 (2) p247-53, ISSN 0007-0920 Journal Code: AV4

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/16 (Item 16 from file: 155)

08445115 93155115

Amphiregulin induces tyrosine phosphorylation of the epidermal growth factor receptor and p185erbB2. Evidence that amphiregulin acts exclusively through the epidermal growth factor receptor at the surface of human epithelial cells.

Johnson GR; Kannan B; Shoyab M; Stromberg K

Laboratory of Cell Biology, Food and Drug Administration, Bethesda, Maryland 20892.

J Biol Chem (UNITED STATES) Feb 5 1993, 268 (4) p2924-31, ISSN 0021-9258 Journal Code: HIV

Languages: ENGLISH

Document type: JOURNAL ARTICLE

3/3/17 (Item 17 from file: 155)

08414553 93124553

Induction of renal adenocarcinoma by a nonmutated erbB oncogene

Taglienti-Sian CA; Banner B; Davis RJ; Robinson HL

Department of Molecular Genetics and Microbiology, University of

Language: ENGLISH

Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL

3/3/7 (Item 7 from file: 155)

08512073 93222073

Schwann cell lineage-specific neu (erbB-2) gene expression in the developing rat nervous system.

Jin JJ; Nikitin AY; Rajewsky MF

Institute of Cell Biology (Cancer Research), University of Essen Medical School, Germany.

Cell Growth Differ (UNITED STATES) Mar 1993, 4 (3) p227-37, ISSN 1044-9523 Journal Code: AYH

Language: ENGLISH

Document type: JOURNAL ARTICLE

3/3/8 (Item 8 from file: 155)

08496095 93206095

Activation of a phosphotyrosine phosphatase by tyrosine phosphorylation.

Vogel W; Lammers R; Huang J; Ullrich A

Department of Molecular Biology, Max-Planck-Institut fur Biochemie, Martinsried, Germany.

Science (UNITED STATES) Mar 12 1993, 259 (5101) p1611-4, ISSN 0036-8075 Journal Code: UJ7

Language: ENGLISH

Document type: JOURNAL ARTICLE

3/3/9 (Item 9 from file: 155)

08494970 93204970

A truncated intracellular HER2/neu receptor produced by alternative RNA processing affects growth of human carcinoma cells.

Scott GK; Robles R; Park JW; Montgomery PA; Daniel J; Holmes WE; Lee J; Keller GA; Li WL; Fendly BM; et al

Cancer Research Institute, University of California, San Francisco 94143-0128.

Mol Cell Biol (UNITED STATES) Apr 1993, 13 (4) p2247-57, ISSN 0270-7306 Journal Code: NGY

Contract/Grant No.: CA-44768, CA, NCI; CA-36773, CA, NCI

Language: ENGLISH

Document type: JOURNAL ARTICLE

3/3/10 (Item 10 from file: 155)

08493131 93203131

The role of erbB-2 and its ligands in growth control of malignant breast epithelium.

Lupu R; Dickson RB; Lippman ME

Lombardi Cancer Research Center, Georgetown University Medical Center, Washington, DC 20007.

Princess Takamatsu Symp (UNITED STATES) 1991, 22 p49-60, Journal Code: HHI

Language: ENGLISH

Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL

3/3/11 (Item 11 from file: 155)

08489253 93199253

Human lung cancers growing on extracellular matrix: expression of oncogenes and growth factors.

Pavelic K; Antonic M; Pavelic L; Pavelic J; Pavelic Z; Spaventi S

Ruder Boskovic Institute, Laboratory of Molecular Oncology, Zagreb, Croatia.

Anticancer Res (GREECE) Nov-Dec 1992, 12 (6B) p2191-6, ISSN 0250-7005 Journal Code: 59L

Language: ENGLISH

Document type: JOURNAL ARTICLE

3/3/12 (Item 12 from file: 155)

08482520 93192520

University of Southern California School of Medicine 90054-0700.  
J Biol Chem (UNITED STATES) Aug 25 1993, 268 (24) p18213-7, ISSN  
0021-9258 Journal Code: HIV  
Languages: ENGLISH  
Document type: JOURNAL ARTICLE

3/3/2 (Item 2 from file: 155)  
08641159 93351159  
Differential responses of human tumor cell lines to anti-p185HER2  
monoclonal antibodies.  
Lewis GD; Figari I; Fendly B; Wong WL; Carter P; Gorman C; Shepard HM  
Genentech Inc., South San Francisco, CA 94080.  
Cancer Immunol Immunother (GERMANY) Sep 1993, 37 (4) p255-63, ISSN  
0340-7004 Journal Code: CN3  
Languages: ENGLISH  
Document type: JOURNAL ARTICLE

3/3/3 (Item 3 from file: 155)  
08638268 93348268  
Substitution of the erbB-2 oncoprotein transmembrane domain activates the  
insulin receptor and modulates the action of insulin and insulin-receptor  
substrate 1.  
Cheatham B; Shoelson SE; Yamada K; Goncalves E; Kahn CR  
Joslin Diabetes Center, Department of Medicine, Brigham and Women's  
Hospital, Harvard Medical School, Boston, MA 02215.  
Proc Natl Acad Sci U S A (UNITED STATES) Aug 1 1993, 90 (15) p7336-40,  
ISSN 0027-8424 Journal Code: PV3  
Contract/Grant No.: DK31036, DK, NIDDK; DK43123, DK, NIDDK; DK36836, DK,  
NIDDK  
Languages: ENGLISH  
Document type: JOURNAL ARTICLE

3/3/4 (Item 4 from file: 155)  
08636103 93346103  
Characterization of cytotoxic activity of saporin anti-gp185/HER-2  
immunotoxins.  
Tecce R; Digiesi G; Savarese A; Trizio D; Natali PG  
Laboratory of Immunology, Regina Elena Cancer Institute, Rome, Italy.  
Int J Cancer (UNITED STATES) Aug 19 1993, 55 (1) p122-7, ISSN  
0020-7136 Journal Code: GQU  
Languages: ENGLISH  
Document type: JOURNAL ARTICLE

3/3/5 (Item 5 from file: 155)  
08562248 93272248  
Antibody-induced activation of p185HER2 in the human lung adenocarcinoma  
cell line Calu-3 requires bivalency.  
Srinivas U; Tagliabue E; Campiglio M; Menard S; Colnaghi MI  
Division of Experimental Oncology E, Istituto Nazionale Tumori, Milan,  
Italy.  
Cancer Immunol Immunother (GERMANY) Jun 1993, 36 (6) p397-402, ISSN  
0340-7004 Journal Code: CN3  
Languages: ENGLISH  
Document type: JOURNAL ARTICLE

3/3/6 (Item 6 from file: 155)  
08542428 93252428  
The bacterial and mouse mammary tumor virus superantigens; two different  
families of proteins with the same functions.  
Marrack P; Winslow GM; Choi Y; Scherer M; Pullen A; White J; Kappler JW  
Howard Hughes Medical Institute, National Jewish Center for Immunology  
and Respiratory Medicine, Denver, CO.  
Immunol Rev (DENMARK) Feb 1993, 131 p79-92, ISSN 0105-2890  
Journal Code: GG4  
Contract/Grant No.: AI-18780, AI, NIAID; AI-22259, AI, NIAID; AI-17134,

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